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* * * * * * * * * Welcome to STN International * * * * * * * * *

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NEWS 7 FEB 11 WTEXTILES reloaded and enhanced
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NEWS 12 FEB 23 TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
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NEWS 15 MAR 06 INPADOCDB and INPAFAMDB enhanced with new display formats
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NEWS 18 MAR 20 CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS 19 MAR 23 CA/CAplus enhanced with more than 250,000 patent equivalents from China
NEWS 20 MAR 30 IMSPATENTS reloaded and enhanced
NEWS 21 APR 03 CAS coverage of exemplified prophetic substances enhanced
NEWS 22 APR 07 STN is raising the limits on saved answers
NEWS 23 APR 24 CA/CAplus now has more comprehensive patent assignee information
NEWS 24 APR 26 USPATFULL and USPAT2 enhanced with patent assignment/reassignment information
NEWS 25 APR 28 CAS patent authority coverage expanded
NEWS 26 APR 28 ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 27 APR 28 Limits doubled for structure searching in CAS

REGISTRY

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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FILE 'HOME' ENTERED AT 14:33:15 ON 06 MAY 2009

FILE 'CASREACT' ENTERED AT 14:33:53 ON 06 MAY 2009
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FILE CONTENT:1840 - 3 May 2009 VOL 150 ISS 19

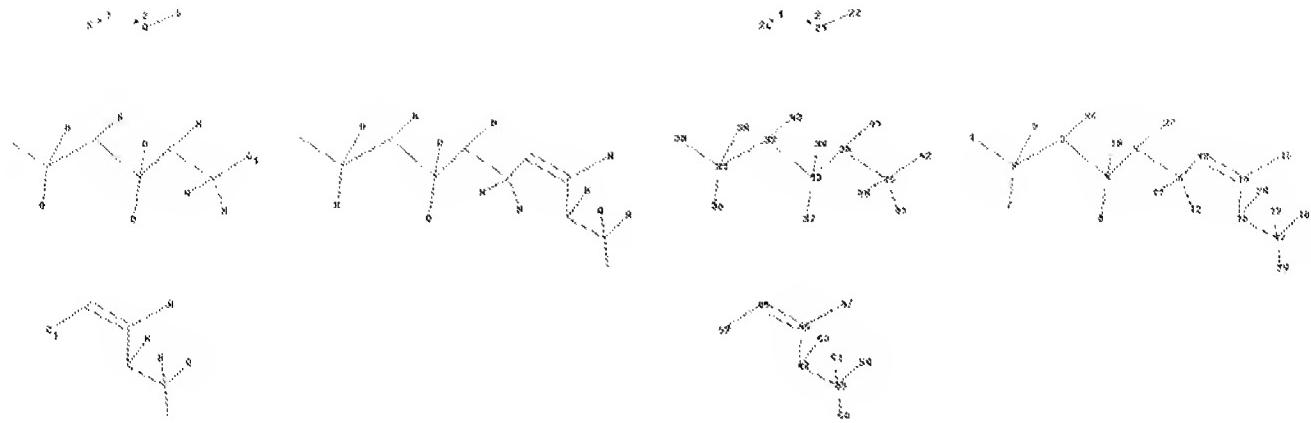
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```
*****  
*  
*      CASREACT now has more than 16.5 million reactions  
*  
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```

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\STNEXP\Queries\10575136.str



```

chain nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 26
27 28 29 30 31 32 33 34 35 37 38 39 40 41 42 43 44 45 46 47 48
49 50 51 52
53 54
ring/chain nodes :
36
chain bonds :
1-2 2-3 2-7 2-9 3-4 3-26 4-5 4-8 4-10 5-6 5-27 6-11 6-12 6-13 13-14
14-15 14-16 16-17 16-28 17-18 17-19 17-29 21-22 30-31 31-32 31-36 31-38
32-33 32-43
33-34 33-37 33-39 34-35 34-44 35-40 35-41 35-42 45-46 45-52 46-47 46-48
48-49 48-53
49-50 49-51 49-54
exact/norm bonds :
2-7 4-8 17-18 21-22 31-36 33-37 35-42 45-52 49-50
exact bonds :
1-2 2-3 2-9 3-4 3-26 4-5 4-10 5-6 5-27 6-11 6-12 6-13 13-14 14-15 14-
16
16-17 16-28 17-19 17-29 30-31 31-32 31-38 32-33 32-43 33-34 33-39 34-35
34-44 35-40
35-41 45-46 46-47 46-48 48-49 48-53 49-51 49-54

G1:[*1], [*2]

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS
31:CLASS 32:CLASS
33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS
51:CLASS 52:CLASS
53:CLASS 54:CLASS
fragments assigned product role:

```

containing 1
fragments assigned reactant/reagent role:
containing 30
containing 45
node mappings:
6:35 13:45

L1 STRUCTURE UPLOADED

```
=> s sss 11
SAMPLE SEARCH INITIATED 14:34:24 FILE 'CASREACT'
SCREENING COMPLETE -      835 REACTIONS TO VERIFY FROM      29 DOCUMENTS
100.0% DONE      835 VERIFIED      0 HIT RXNS      0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:    14968 TO    18432
PROJECTED ANSWERS:          0 TO      0
```

L2 0 SEA SSS SAM L1 (0 REACTIONS)

```
=> d 11
L1 HAS NO ANSWERS
L1      STR
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
Structure attributes must be viewed using STN Express query preparation.
```

```
=> s sss 11 full
FULL SEARCH INITIATED 14:39:59 FILE 'CASREACT'
SCREENING COMPLETE -      21014 REACTIONS TO VERIFY FROM      671 DOCUMENTS
100.0% DONE      21014 VERIFIED      182 HIT RXNS (      6 INCOMP)      9 DOCS
SEARCH TIME: 00.00.05
```

L3 9 SEA SSS FUL L1 (182 REACTIONS)

```
=> d scan
L3      9 ANSWERS      CASREACT      COPYRIGHT 2009 ACS on STN
```

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 9 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Preparation of discodermolide analogs for use in pharmaceutical compositions as antiproliferative agents

RX(12) OF 136 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d 13 1

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

RX(33) OF 320 - REACTION DIAGRAM NOT AVAILABLE

=> d 13 occ 1-9

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	4
NUMBER OF REACTIONS IN PATH	1
NUMBER OF REACTIONS IN SPATH	2
FIELD	COUNT
RX(33)	3
RX(69)	3
RX(132)	3
RX(136)	3

L3 ANSWER 2 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	15
NUMBER OF REACTIONS IN PATH	3
NUMBER OF REACTIONS IN SPATH	4
FIELD	COUNT
RX(12)	3
RX(42)	3
RX(69)	3
RX(71)	3
RX(98)	3
RX(100)	3
RX(103)	3
RX(113)	3
RX(114)	3
RX(115)	3
RX(130)	3
RX(131)	3
RX(132)	3
RX(135)	3
RX(136)	3

L3 ANSWER 3 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	17
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	3
FIELD	COUNT
RX(1)	3
RX(18)	3
RX(31)	3
RX(41)	3
RX(55)	3
RX(78)	3
RX(81)	3
RX(88)	3
RX(89)	3

RX(99)	3	(INCOMPLETE)
RX(100)	3	
RX(106)	3	(INCOMPLETE)
RX(111)	3	(INCOMPLETE)
RX(115)	3	
RX(117)	3	(INCOMPLETE)
RX(118)	3	(INCOMPLETE)
RX(119)	3	(INCOMPLETE)

L3 ANSWER 4 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	30	
NUMBER OF REACTIONS IN PATH	2	
NUMBER OF REACTIONS IN SPATH	4	
FIELD	COUNT	
RX(20)	3	
RX(27)	3	
RX(55)	3	
RX(62)	3	
RX(104)	3	
RX(107)	3	
RX(116)	3	
RX(119)	3	
RX(151)	3	
RX(152)	3	
RX(153)	3	
RX(154)	3	
RX(155)	3	
RX(156)	3	
RX(164)	3	
RX(165)	3	
RX(174)	3	
RX(190)	3	
RX(201)	3	
RX(209)	3	
RX(217)	3	
RX(218)	3	
RX(219)	3	
RX(220)	3	
RX(236)	3	
RX(237)	3	
RX(238)	3	
RX(248)	3	
RX(254)	3	
RX(258)	3	
NUMBER OF HIT REACTIONS	30	
NUMBER OF REACTIONS IN PATH	2	
NUMBER OF REACTIONS IN SPATH	4	

L3 ANSWER 5 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	36	
NUMBER OF REACTIONS IN PATH	4	
NUMBER OF REACTIONS IN SPATH	6	
FIELD	COUNT	
RX(13)	3	
RX(17)	3	
RX(21)	3	
RX(39)	3	
RX(43)	3	

RX(46)	3
RX(47)	3
RX(73)	3
RX(79)	3
RX(80)	3
RX(81)	3
RX(82)	3
RX(84)	3
RX(85)	3
RX(86)	3
RX(87)	3
RX(88)	3
RX(89)	3
RX(91)	3
RX(93)	3
RX(136)	3
RX(137)	3
RX(138)	3
RX(139)	3
RX(140)	3
RX(141)	3
RX(142)	3
RX(143)	3
RX(144)	3
RX(145)	3
RX(146)	3
RX(147)	3
RX(148)	3
RX(149)	3
RX(150)	3
RX(151)	3
NUMBER OF HIT REACTIONS	36
NUMBER OF REACTIONS IN PATH	4
NUMBER OF REACTIONS IN SPATH	6

L3 ANSWER 6 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

	COUNT
NUMBER OF HIT REACTIONS	21
NUMBER OF REACTIONS IN PATH	6
NUMBER OF REACTIONS IN SPATH	7
FIELD	COUNT
RX(35)	3
RX(39)	3
RX(41)	3
RX(75)	3
RX(81)	3
RX(150)	3
RX(151)	3
RX(154)	3
RX(157)	3
RX(313)	3
RX(314)	3
RX(382)	3
RX(398)	3
RX(503)	3
RX(504)	3
RX(507)	3
RX(508)	3
RX(529)	3
RX(530)	3

RX(567)	3
RX(568)	3
NUMBER OF HIT REACTIONS	21
NUMBER OF REACTIONS IN PATH	6
NUMBER OF REACTIONS IN SPATH	7

L3 ANSWER 7 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	2
NUMBER OF REACTIONS IN PATH	1
NUMBER OF REACTIONS IN SPATH	2
FIELD	COUNT
RX(17)	3
RX(33)	3

L3 ANSWER 8 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

NUMBER OF HIT REACTIONS	56
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	2
FIELD	COUNT
RX(11)	3
RX(44)	3
RX(61)	3
RX(87)	3
RX(89)	3
RX(115)	3
RX(116)	3
RX(121)	3
RX(122)	3
RX(123)	3
RX(124)	3
RX(125)	3
RX(127)	3
RX(175)	3
RX(178)	3
RX(179)	3
RX(180)	3
RX(181)	3
RX(222)	3
RX(226)	3
RX(227)	3
RX(230)	3
RX(231)	3
RX(232)	3
RX(238)	3
RX(239)	3
RX(240)	3
RX(241)	3
RX(242)	3
RX(243)	3
RX(244)	3
RX(245)	3
RX(246)	3
RX(247)	3
RX(248)	3
RX(249)	3
RX(250)	3
RX(252)	3
RX(304)	3

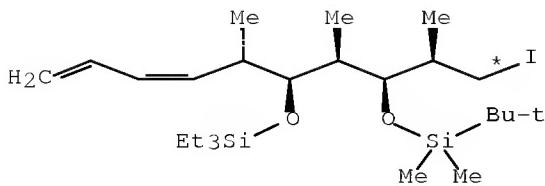
RX(306)	3
RX(308)	3
RX(310)	3
RX(312)	3
RX(314)	3
RX(316)	3
RX(318)	3
RX(320)	3
RX(322)	3
RX(324)	3
RX(326)	3
RX(348)	3
RX(349)	3
RX(350)	3
RX(351)	3
RX(352)	3
RX(353)	3
NUMBER OF HIT REACTIONS	56
NUMBER OF REACTIONS IN PATH	2
NUMBER OF REACTIONS IN SPATH	2

L3 ANSWER 9 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
 NUMBER OF HIT REACTIONS 1
 NUMBER OF REACTIONS IN PATH 1
 NUMBER OF REACTIONS IN SPATH 1
 FIELD COUNT
 RX(5) 3

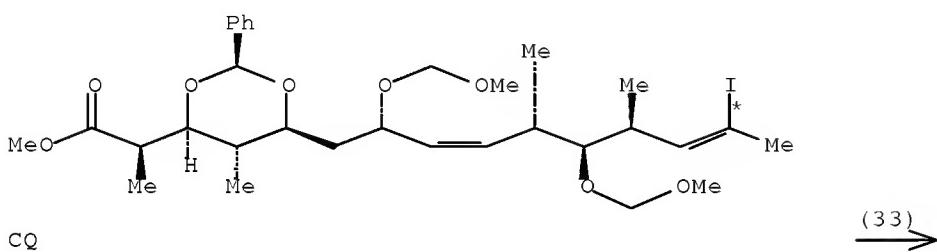
=> d ibib abs hit 13 1-9

L3 ANSWER 1 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 147:52745 CASREACT Full-text
 TITLE: α -Oxygenated crotyltitanium and dyotropic rearrangement in the total synthesis of discodermolide
 AUTHOR(S): de Lemos, Elsa; Poree, Francois-Hugues; Commercon, Alain; Betzer, Jean-Francois; Pancrazi, Ange; Ardisson, Janick
 CORPORATE SOURCE: CNRS UMR 8123, Universite de Cergy-Pontoise, Cergy Pontoise, 95031, Fr.
 SOURCE: Angewandte Chemie, International Edition (2007), 46(11), 1917-1921
 CODEN: ACIEF5; ISSN: 1433-7851
 PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The total synthesis of discodermolide relies on the elaboration of syn-anti stereotriads linked to a Z-O-enecarbamate group, its direct transformation into the terminal Z diene, and stereocontrolled generation of the trisubstituted Z double bond by a dyotropic rearrangement. The synthesis was achieved in 21 steps with 1.6% overall yield.
 REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(33) OF 320 ...BZ + CQ ==> CU...



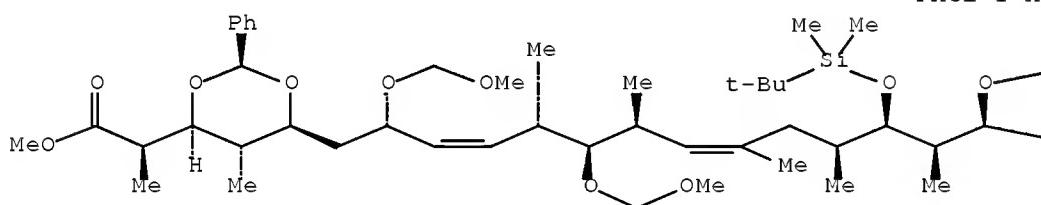
BZ



CQ

$\xrightarrow{(33)}$

PAGE 1-A



PAGE 1-B

---SiEt_3



CU
YIELD 60%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi
 SOL 75-65-0 t-BuOH
 CON SUBSTAGE(1) -80 deg C
 SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

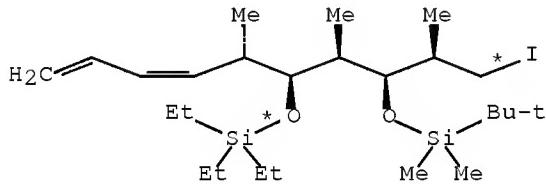
RGT CV 280-64-8 9-BBN
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, -80 deg C
 SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

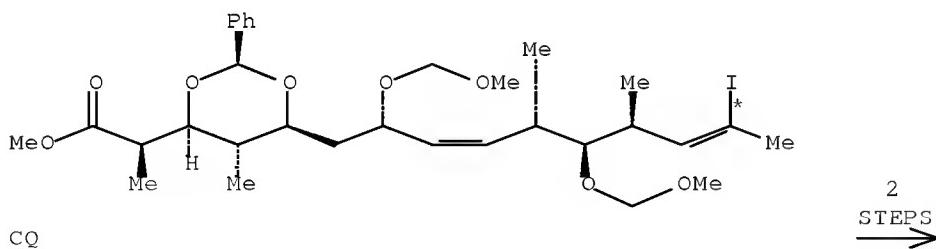
RCT CQ 939795-51-4
 RGT CW 534-17-8 Cs₂CO₃
 SOL 68-12-2 DMF
 CON 16 hours, room temperature

PRO CU 939795-52-5

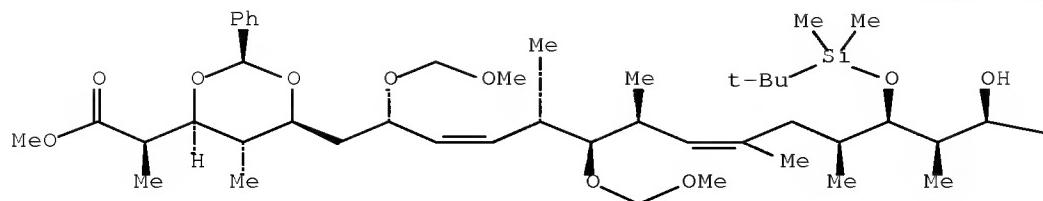
RX(69) OF 320 COMPOSED OF RX(33), RX(34)
 RX(69) BZ + CQ ==> CX



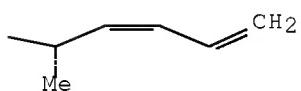
BZ



PAGE 1-A



PAGE 1-B



CX
YIELD 77%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi
SOL 75-65-0 t-BuOH
CON SUBSTAGE(1) -80 deg C
SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 minutes, -80 deg C
SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

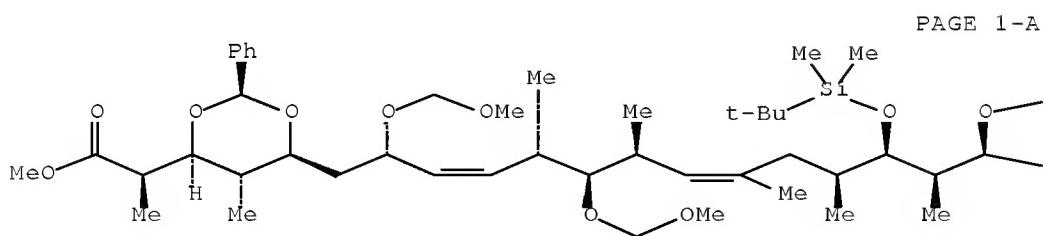
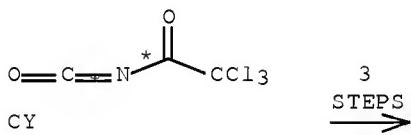
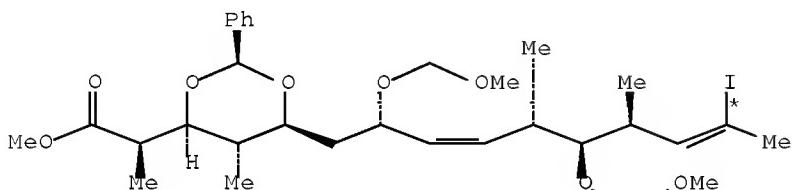
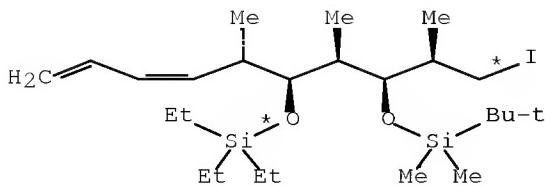
STAGE(3)

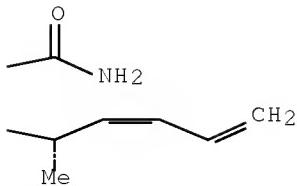
RCT CQ 939795-51-4
RGT CW 534-17-8 Cs₂CO₃
SOL 68-12-2 DMF
CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5
RGT I 104-15-4 TsOH
PRO CX 939795-64-9
SOL 67-56-1 MeOH
CON 1 hour, 0 deg C

RX(132) OF 320 COMPOSED OF RX(33), RX(34), RX(35)
RX(132) BZ + CQ + CY ==> CZ





CZ
YIELD 64%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi
 SOL 75-65-0 t-BuOH
 CON SUBSTAGE(1) -80 deg C
 SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 10 minutes, -80 deg C
 SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

RCT CQ 939795-51-4
 RGT CW 534-17-8 Cs₂CO₃
 SOL 68-12-2 DMF
 CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5
 RGT I 104-15-4 TsOH
 PRO CX 939795-64-9
 SOL 67-56-1 MeOH
 CON 1 hour, 0 deg C

RX(35) RCT CX 939795-64-9, CY 3019-71-4

STAGE(1)

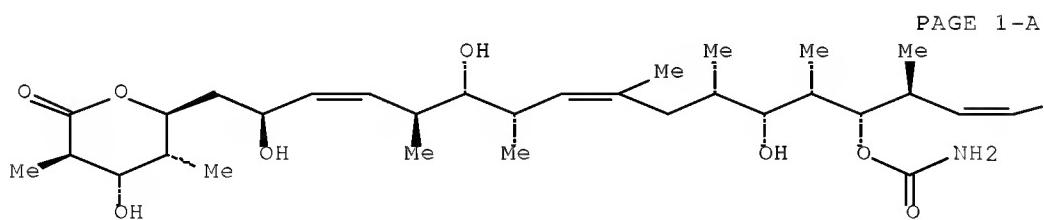
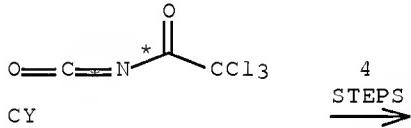
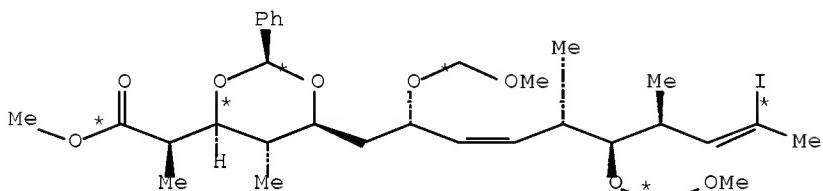
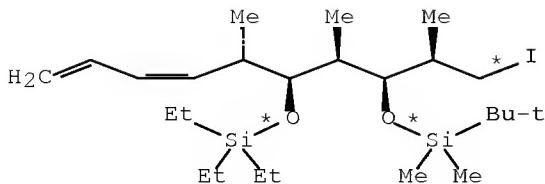
SOL 75-09-2 CH₂Cl₂
 CON 15 minutes, room temperature

STAGE(2)

RGT DA 584-08-7 K₂CO₃
 SOL 67-56-1 MeOH
 CON 1.5 hours, room temperature

PRO CZ 939795-65-0

RX(136) OF 320 COMPOSED OF RX(33), RX(34), RX(35), RX(36)
 RX(136) BZ + CQ + CY ==> DB



PAGE 1-B



DB
YIELD 70%

RX(33) RCT BZ 649755-91-9

STAGE(1)

RGT O 594-19-4 t-BuLi
SOL 75-65-0 t-BuOH
CON SUBSTAGE(1) -80 deg C
SUBSTAGE(2) 2 minutes, -80 deg C

STAGE(2)

RGT CV 280-64-8 9-BBN
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 minutes, -80 deg C
SUBSTAGE(2) 75 minutes, -80 deg C -> room temperature

STAGE(3)

RCT CQ 939795-51-4
RGT CW 534-17-8 Cs₂CO₃
SOL 68-12-2 DMF
CON 16 hours, room temperature

PRO CU 939795-52-5

RX(34) RCT CU 939795-52-5
RGT I 104-15-4 TsOH
PRO CX 939795-64-9
SOL 67-56-1 MeOH
CON 1 hour, 0 deg C

RX(35) RCT CX 939795-64-9, CY 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 15 minutes, room temperature

STAGE(2)

RGT DA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON 1.5 hours, room temperature

PRO CZ 939795-65-0

RX(36) RCT CZ 939795-65-0
RGT DC 7647-01-0 HCl
PRO DB 127943-53-7
SOL 109-99-9 THF
CON 72 hours, room temperature

L3 ANSWER 2 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 144:467954 CASREACT Full-text

TITLE: Preparation of discodermolide analogs for use in pharmaceutical compositions as antiproliferative agents

INVENTOR(S): Sundermann, Kurt F.; Shaw, Simon James; Santi, Daniel V.

PATENT ASSIGNEE(S): Kosan Biosciences Incorporated, USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

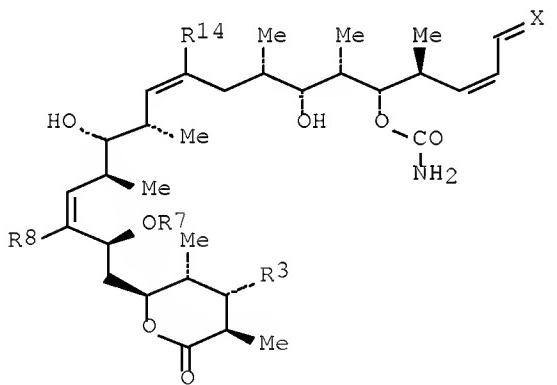
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060106094	A1	20060518	US 2005-261686	20051028
US 7214708	B2	20070508		
WO 2006055472	A2	20060526	WO 2005-US41126	20051110
WO 2006055472	A3	20070215		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2004-629401P	20041118
			US 2004-629518P	20041118
			US 2004-629519P	20041118
			US 2004-629520P	20041118
			US 2005-261686	20051028

OTHER SOURCE(S): MARPAT 144:467954

GI



I

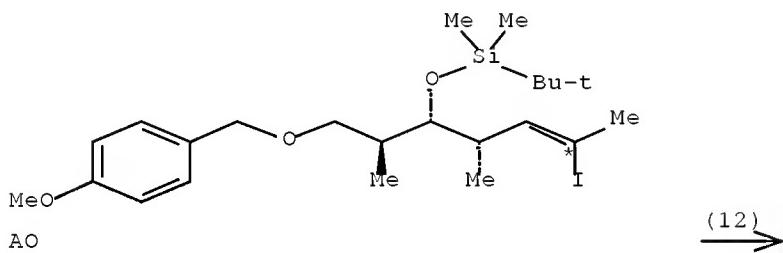
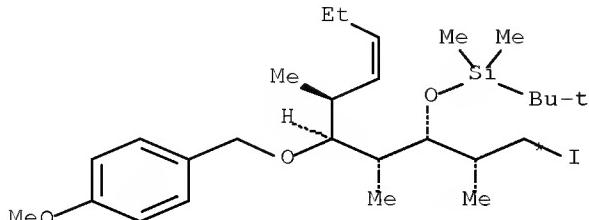
AB Discodermolide analogs, such as I [R3 = OH, R7 = CH2OMe, CH2O(CH2)2OMe, R8 = H, R14 = Me, X = CH2; R3 = OH, R7 = CH2OMe, R8 = R14 = H, X = CH2; R3 = OH, R7 = H, R8 = Me, R14 = Me, X = CH2; R3 = H, OMe, R7 = R8 = H, R14 = Me, X = (H)Me], were prepared for therapeutic use in the treatment of cancer. Discodermolide I (R3 = OH, R7 = R8 = H, R14 = Me, X = CH2) and its prepared analogs were assayed for inhibition of a number of cancer cell lines, such as MCF-7, A549 and SKOV-3.

REFERENCE COUNT:

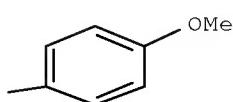
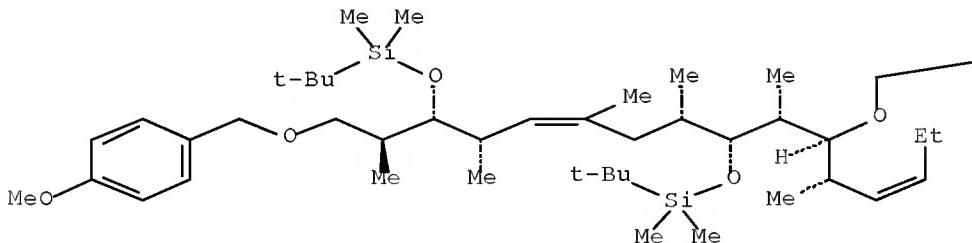
54

THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(12) OF 136 AN + AO ==> AP...



PAGE 1-A



AP
YIELD 70%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature → -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

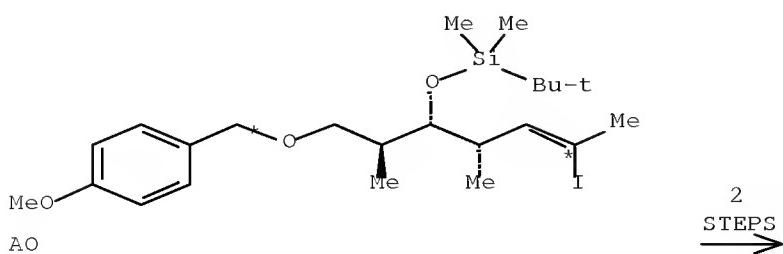
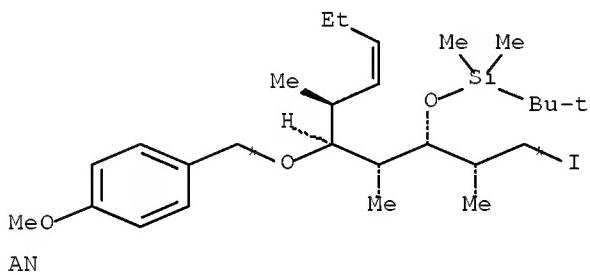
RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

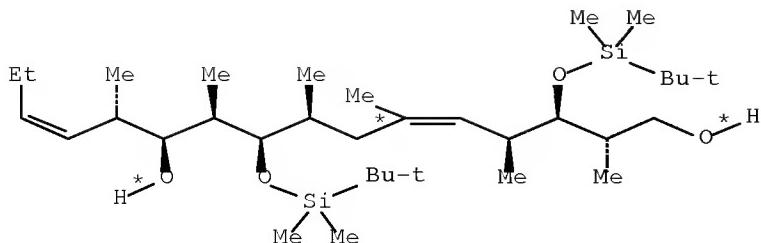
STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(42) OF 136 COMPOSED OF RX(12), RX(13)
RX(42) AN + AO ==> AU





AU
YIELD 63%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

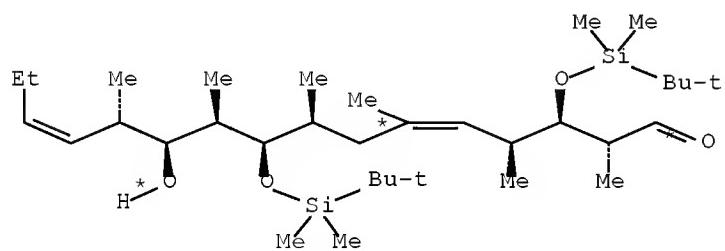
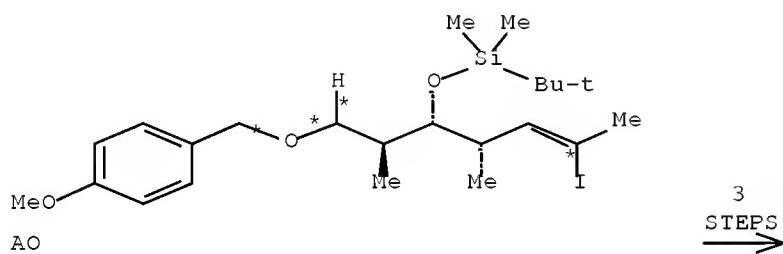
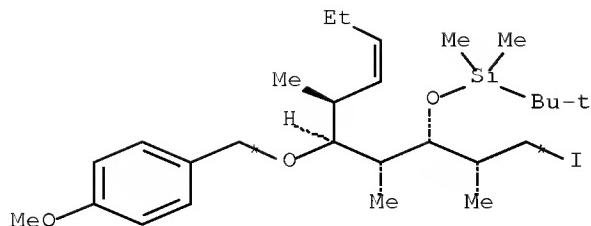
RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(69) OF 136 COMPOSED OF RX(12), RX(13), RX(14)
 RX(69) AN + AO ==> AY



AY
YIELD 77%

RX(12) RCT AN 870075-02-6

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature \rightarrow -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C \rightarrow room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄

CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9

NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

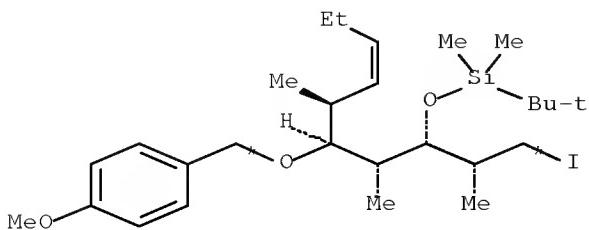
STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

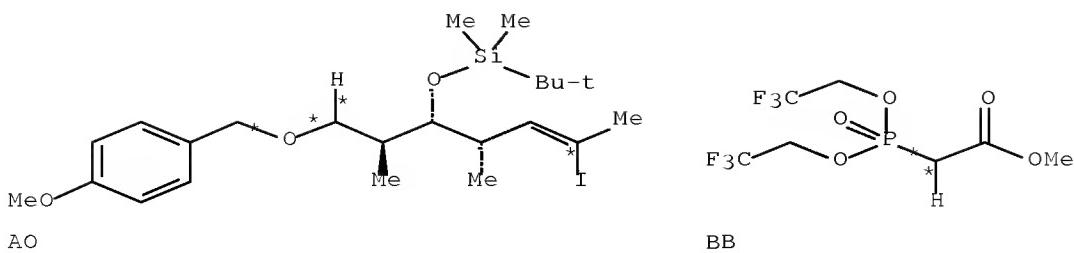
PRO AY 886845-62-1

RX(71) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15)

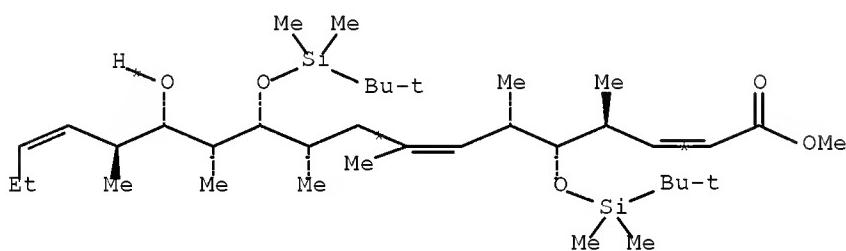
RX(71) AN + AO + BB ==> BC



AN



4
STEPS
→



RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature → -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C → room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

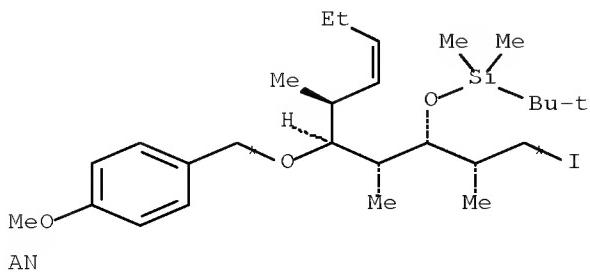
STAGE(2)

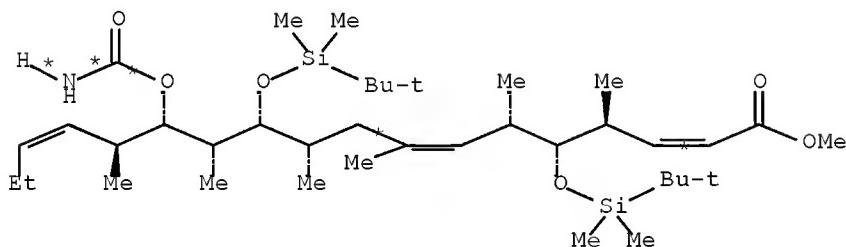
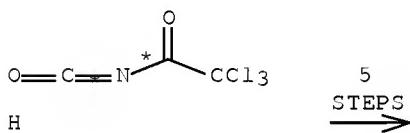
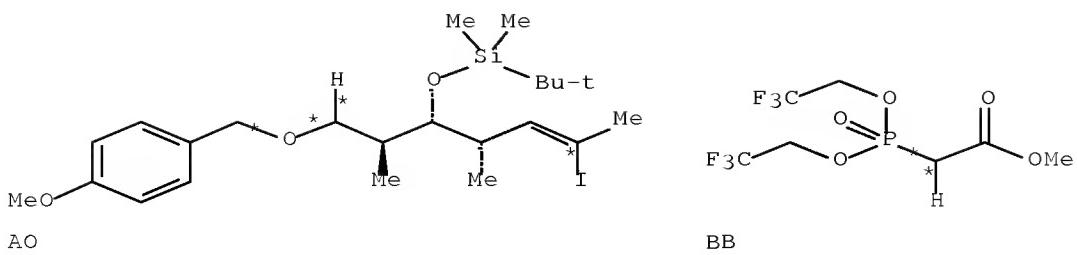
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(98) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16)
RX(98) AN + AO + BB + H ==> BD





BD
YIELD 87%

RX(12) RCT AN 870075-02-8

STAGE (1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature → -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C → room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE (2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)
RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂C₁₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

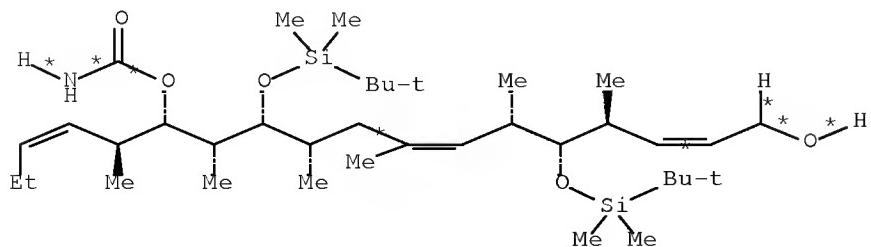
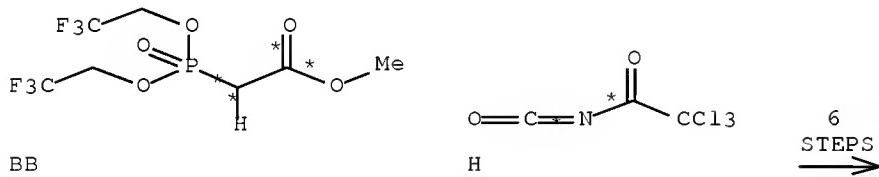
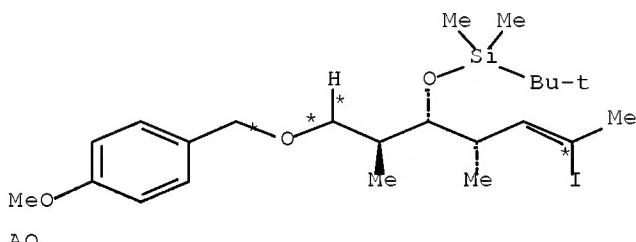
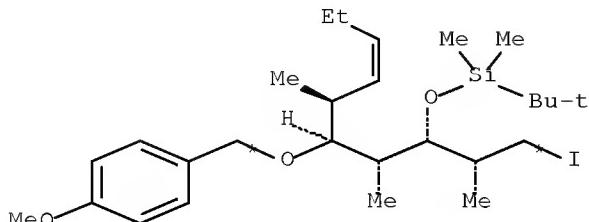
RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845--64--3

RX(100) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17)
RX(100) AN + AO + BB + H ==> AI



AI
YIELD 88%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7

RGT J 584-08-7 K2CO3
 PRO BC 886845-63-2
 CAT 17455-13-9 18-Crown-6
 SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

STAGE(2)
 RGT J 584-08-7 K2CO3
 SOL 67-56-1 MeOH
 CON SUBSTAGE(1) room temperature -> 0 deg C
 SUBSTAGE(2) 1 hour, 0 deg C
 SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

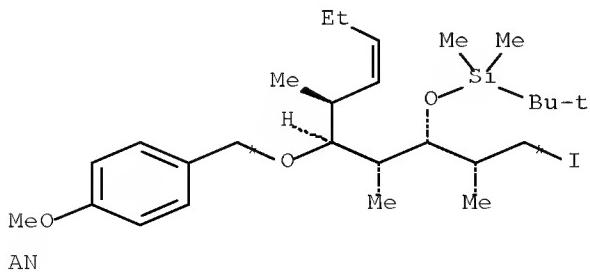
RX(17) RCT BD 886845-64-3

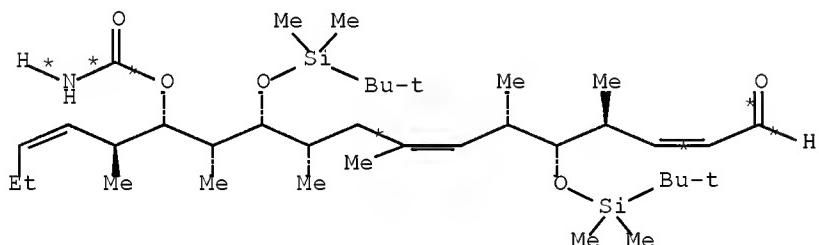
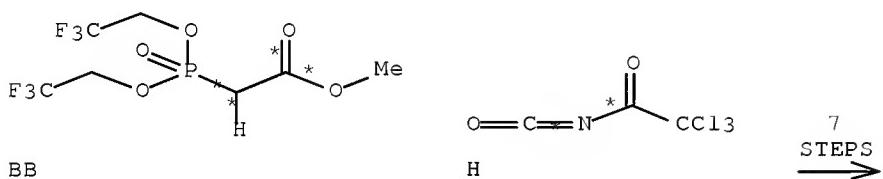
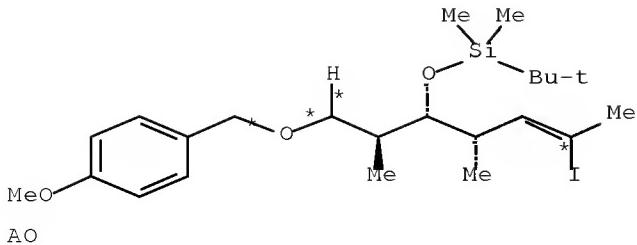
STAGE(1)
 RGT N 1191-15-7 AlH(Bu-i)2
 SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
 CON 25 minutes, -78 deg C

STAGE(2)
 RGT O 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON SUBSTAGE(1) 0 deg C
 SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(103) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
 RX(9)
 RX(103) AN + AO + BB + H ==> AJ





RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature → -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C → room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGD P 7732-18-5 Water

CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

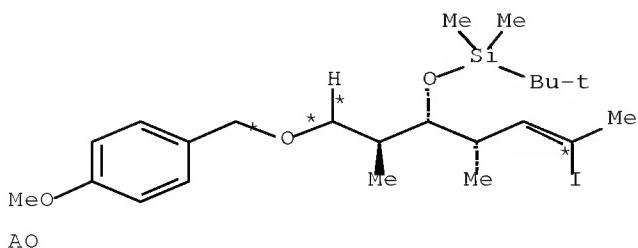
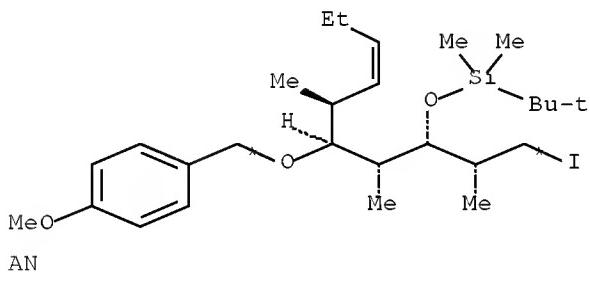
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

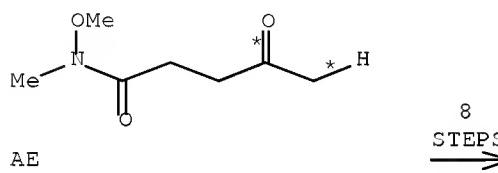
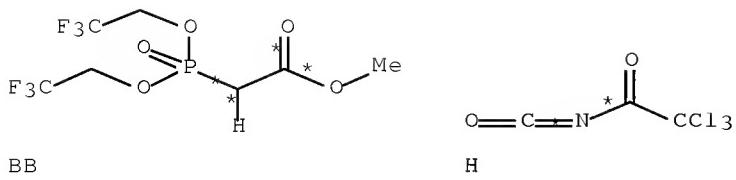
STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

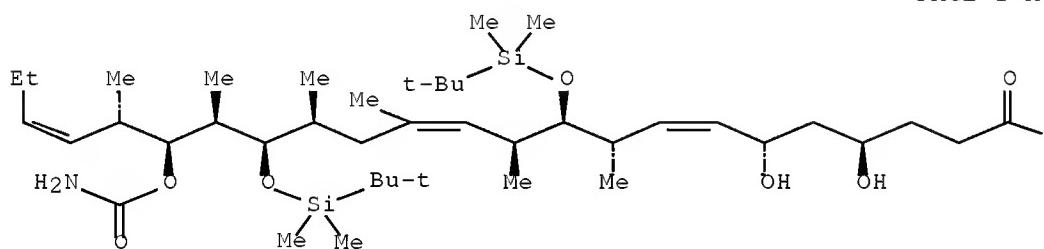
PRO AJ 886845-57-4

RX(113) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10)
RX(113) AN + AO + BB + H + AE ==> AL

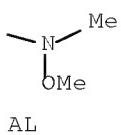




PAGE 1-A



PAGE 1-B



RX(12) RCT AN 870075-02-8

STAGE (1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)
RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RCT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RCT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)
RGT X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)
RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)
RGT L 67-56-1 MeOH

CON 0 deg C

STAGE (4)

RGT Y 7722-84-1 H2O2

SOL 7732-18-5 Water

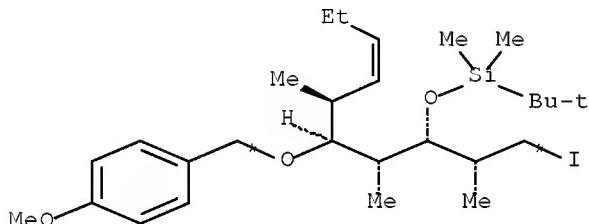
CON 1 hour, room temperature, pH 7

PRO AL 886845-58-5

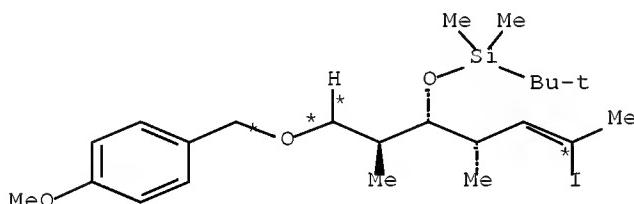
NTE stereoselective, phosphate buffered used in stage 4, Aldol reaction

RX(114) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(18)

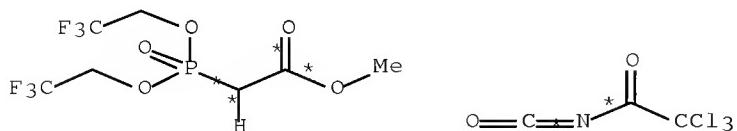
RX(114) AN + AO + BB + H + BF ==> BG



AN

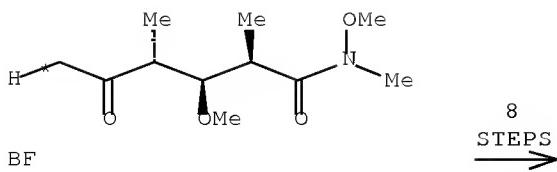


AO

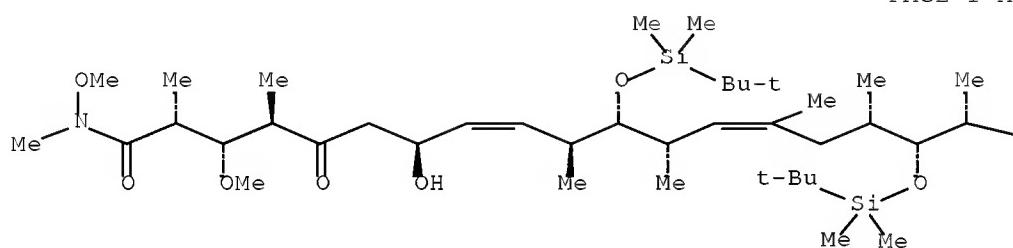


BB

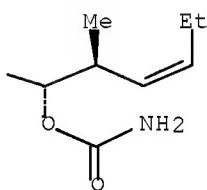
H



PAGE 1-A



PAGE 1-B



BG
YIELD 87%

RX(12) RCT AN 870075-02-8

STAGE (1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE (2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)
RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂C₁₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)
RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

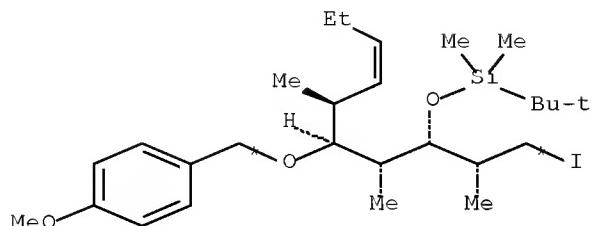
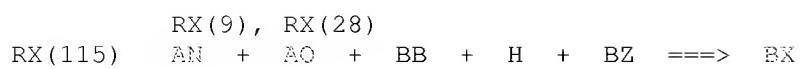
STAGE(2)
RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)
RGT L 67-56-1 MeOH
CON 0 deg C

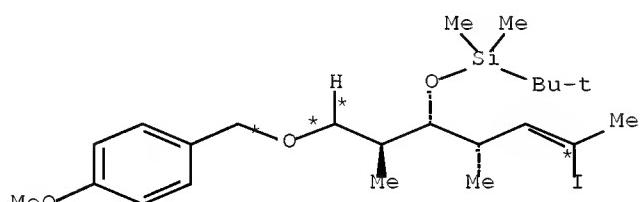
STAGE(4)
RGT Y 7722-84-1 H₂O₂
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BG 886845-66-5
NTE stereoselective, phosphate buffered solution used in stage 4

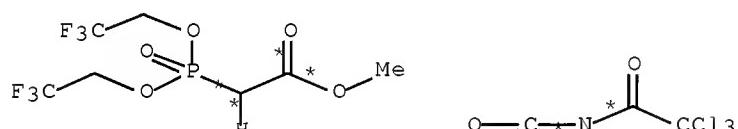
RX(115) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),



AN

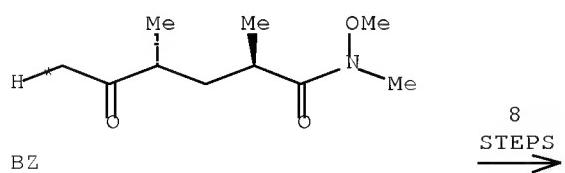


AO



BB

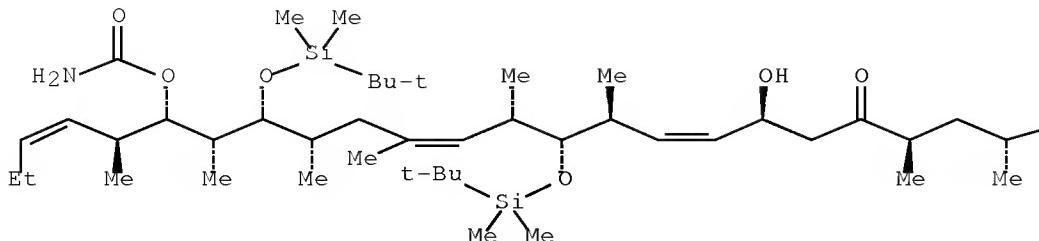
H



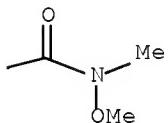
BZ

8 STEPS
→

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BX
YIELD 83%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature → -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9

NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me4-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)

RGT AK 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K2CO3
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)

RGT J 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(28) RCT BZ 884313-63-7

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

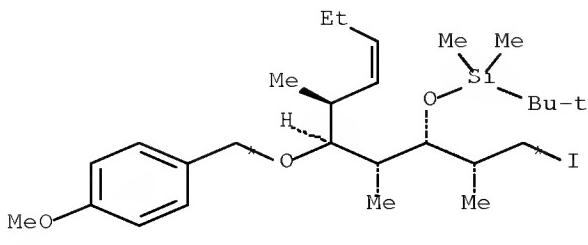
RGT Y 7722-84-1 H₂O₂
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BX 886845-76-7

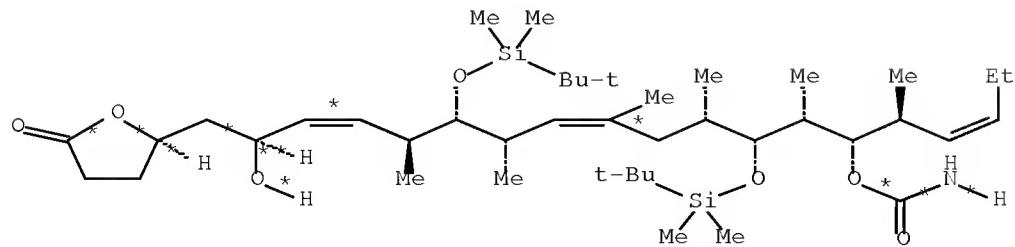
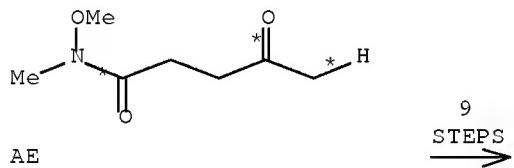
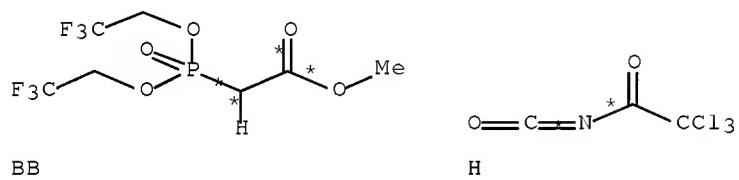
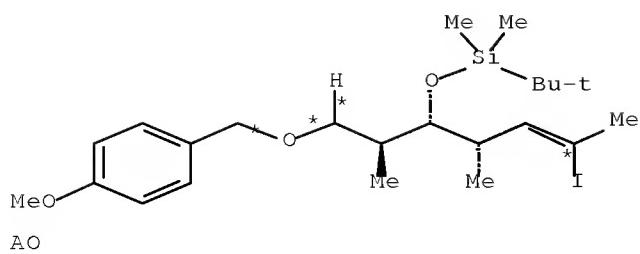
NTE stereoselective, phosphate buffered solution used in stage 4

RX(130) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10), RX(11)

RX(130) AN + AO + BB + H + AE ==> AM



AN



AM
YIELD 22%

RX(12) RCT AN 870075-02-8

STAGE(1)
RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
SOL 60-29-7 Et2O, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 5 minutes, -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AO 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)
RGT P 7732-18-5 Water
CON room temperature

PRO AP 886845-60-9
NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)
RGT AV 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AW 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)

RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)

RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)

RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)

RGT X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO AL 886845-58-5

NTE stereoselective, phosphate buffered used in stage 4, Aldol reaction

RX(11)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT AL 886845-58-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

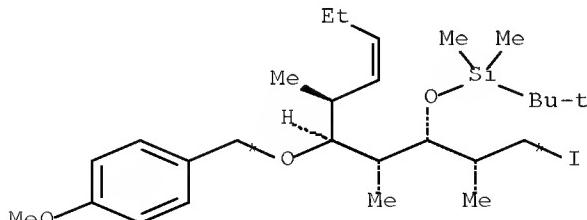
PRO AM 886845-59-6

NTE stereoselective

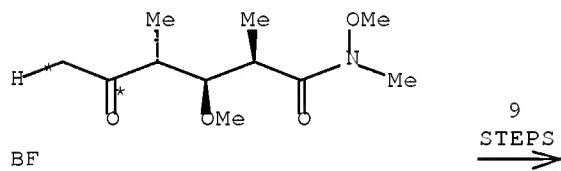
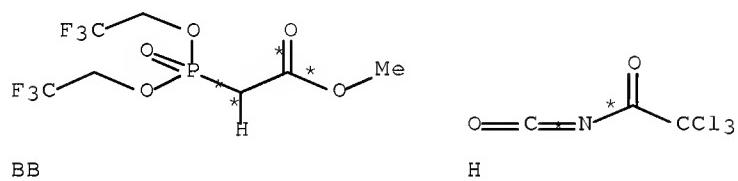
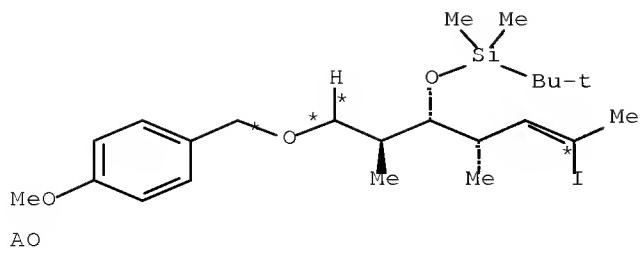
RX(131) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),

RX(9), RX(18), RX(19)

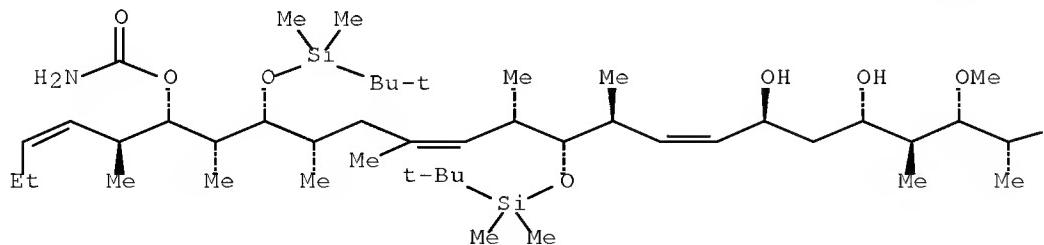
RX(131) AN + AO + BB + H + BF ==> BH

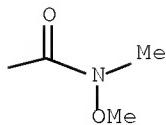


AN



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^{BH}
YIELD 81%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDOQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE (1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE (2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE (1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE (2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE (1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RG T L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BG 886845-66-5

NTE stereoselective, phosphate buffered solution used in stage 4

RX(19)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT BG 886845-66-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

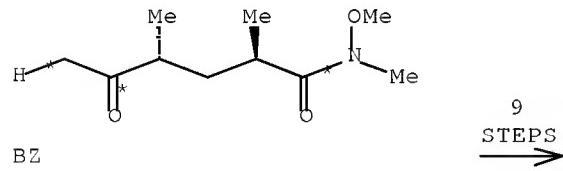
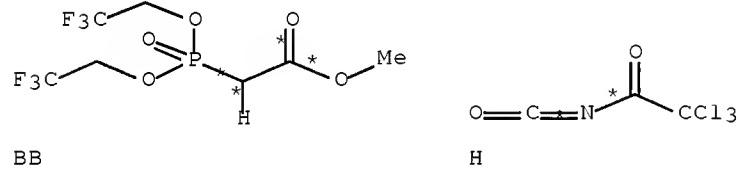
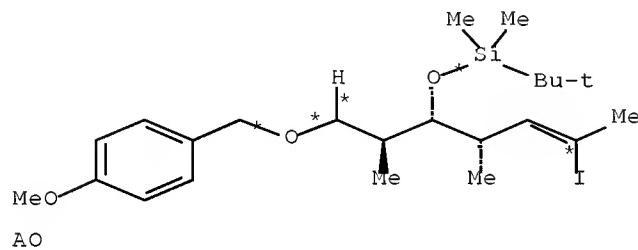
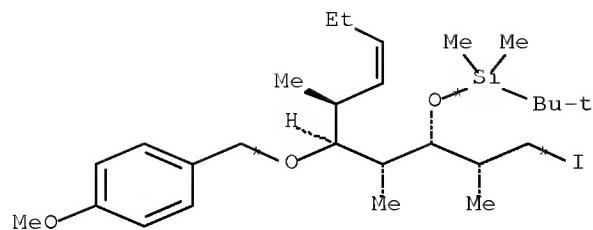
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

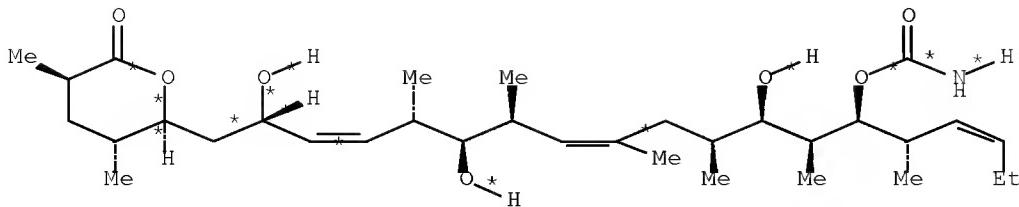
PRO BH 886845-67-6

NTE stereoselective

RX(132) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(28), RX(27)

RX(132) AN + AO + BB + H + BZ ==> BY





BY
YIELD 6%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDOQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE (1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE (2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE (1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE (2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE (1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(28) RCT BZ 884313-63-7

STAGE(1)

RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BX 886845-76-7

NTE stereoselective, phosphate buffered solution used in stage 4

RX(27)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT BX 886845-76-7
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

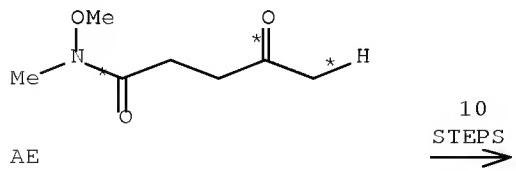
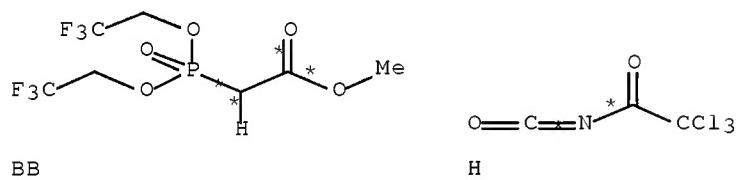
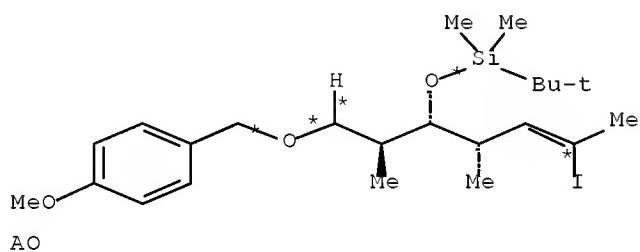
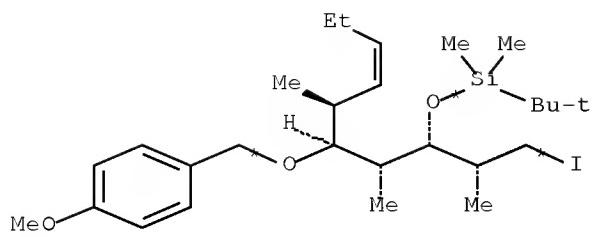
STAGE(4)

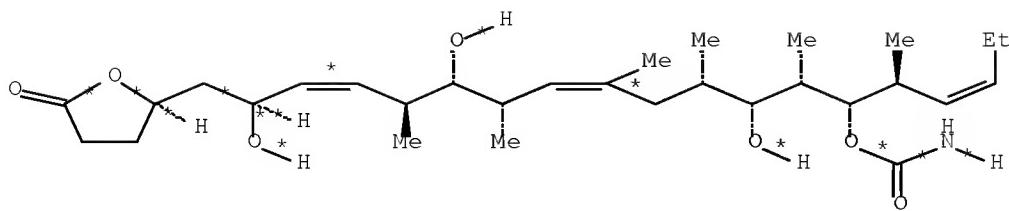
RGT BT 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature

PRO BY 886845-75-6

NTE stereoselective, incremental addition of the reagent in stage 4

RX(135) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
RX(9), RX(10), RX(11), RX(25)
RX(135) AN + AO + BB + H + AE ==> BV





BV
YIELD 57%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT P 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9
 NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDOQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)

RGT AX 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)

RGT AZ 2564-83-2 Me₄-piperidoxyl, BA 1321-07-9 Benzoic acid,

iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K₂CO₃
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE (1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE (2)
RGT J 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE (1)
RGT N 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE (2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE (1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE (2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(10) RCT AE 193805-82-2

STAGE(1)

RGT X 121-44-8 Et3N
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)

RCT AJ 886845-57-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)

RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)

RGT Y 7722-84-1 H2O2
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO AL 886845-58-5

NTE stereoselective, phosphate buffered used in stage 4, Aldol reaction

RX(11)

STAGE(1)

RGT AB 109704-53-2 Me4N.(AcO)3BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

STAGE(2)

RCT AL 886845-58-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

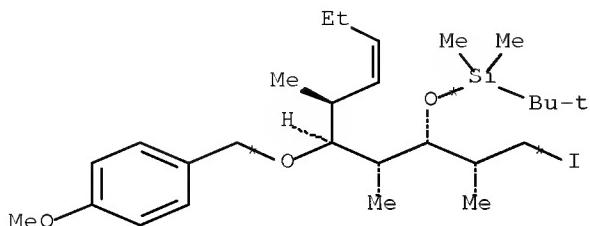
PRO AM 886845-59-6

NTE stereoselective

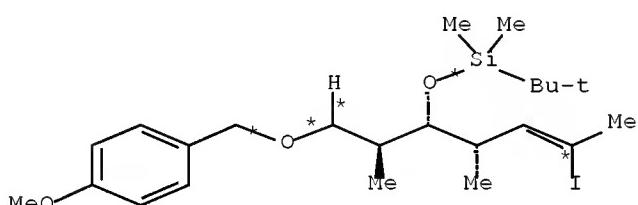
RX(25)

RCT AM 886845-59-6
RGT BT 7647-01-0 HCl
PRO BV 886845-73-4
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature
NTE incremental addition of the reagent

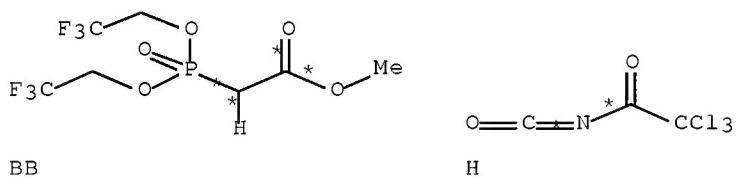
RX(136) OF 136 COMPOSED OF RX(12), RX(13), RX(14), RX(15), RX(16), RX(17),
 RX(9), RX(18), RX(19), RX(26)
 RX(136) AN + AO + BB + H + BF ==> BW



AN

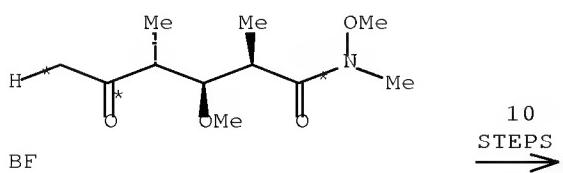


AO



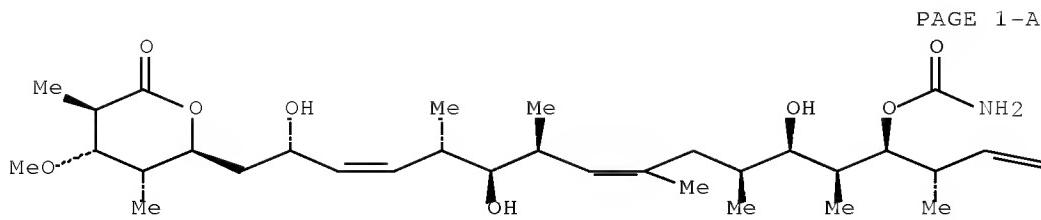
BB

H



BF

10
STEPS
→



PAGE 1-B



^{BW}
YIELD 92%

RX(12) RCT AN 870075-02-8

STAGE(1)

RGT AQ 109-72-8 BuLi, AR 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature → -78 deg C
 SUBSTAGE(2) 5 minutes, -78 deg C
 SUBSTAGE(3) -78 deg C → room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AO 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RG T 7732-18-5 Water
 CON room temperature

PRO AP 886845-60-9

NTE in the dark in stage 2

RX(13) RCT AP 886845-60-9

STAGE(1)

RGT AV 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AW 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes, room temperature

STAGE(3)
RGT AX 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO AU 886845-61-0

RX(14) RCT AU 886845-61-0

STAGE(1)
RGT AZ 2564-83-2 Me4-piperidoxy1, BA 1321-07-9 Benzoic acid,
iodo-
SOL 75-09-2 CH2C12
CON 2.5 hours, room temperature

STAGE(2)
RGT AK 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO AY 886845-62-1

RX(15) RCT AY 886845-62-1, BB 88738-78-7
RGT J 584-08-7 K2CO3
PRO BC 886845-63-2
CAT 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe

RX(16) RCT BC 886845-63-2, H 3019-71-4

STAGE(1)
SOL 75-09-2 CH2C12
CON 1 hour, room temperature

STAGE(2)
RGT J 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 1 hour, 0 deg C
SUBSTAGE(3) 1.5 hours, room temperature

PRO BD 886845-64-3

RX(17) RCT BD 886845-64-3

STAGE(1)
RGT N 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2C12, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 1.5 deg C

PRO AI 886845-65-4

RX(9) RCT AI 886845-65-4

STAGE(1)
RGT S 144-55-8 NaHCO₃, R 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT AK 7772-98-7 Na₂S₂O₃, S 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO AJ 886845-57-4

RX(18) RCT BF 884313-62-6

STAGE(1)
RGT W 112246-73-8 Bicycloheptylborane, X 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> -78 deg C

STAGE(2)
RCT AJ 886845-57-4
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C
SUBSTAGE(3) -20 deg C -> 0 deg C

STAGE(3)
RGT L 67-56-1 MeOH
CON 0 deg C

STAGE(4)
RGT Y 7722-84-1 H₂O₂
SOL 7732-18-5 Water
CON 1 hour, room temperature, pH 7

PRO BG 886845-66-5

NTE stereoselective, phosphate buffered solution used in stage 4

RX(19)

STAGE(1)
RGT AB 109704-53-2 Me₄N.(AcO)₃BH, AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, room temperature
SUBSTAGE(2) room temperature -> -30 deg C

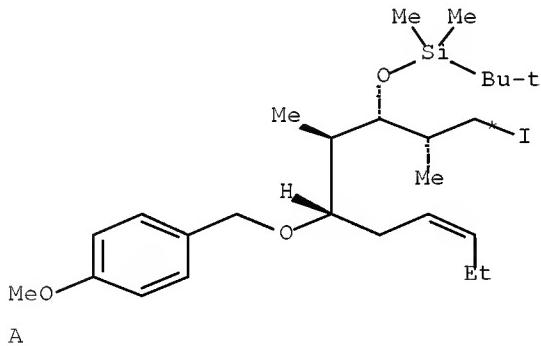
STAGE(2)
RCT BG 886845-66-5
RGT AC 64-19-7 AcOH
SOL 75-05-8 MeCN
CON SUBSTAGE(1) 30 minutes, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

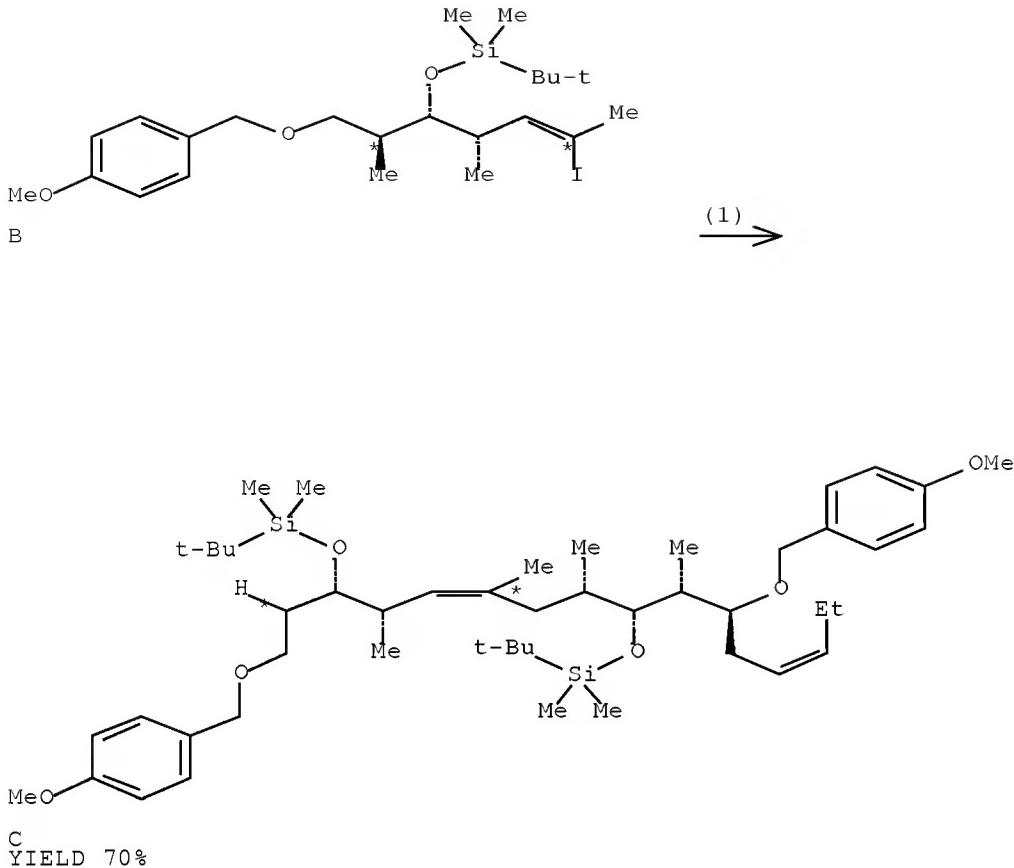
STAGE(3)
RGT O 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO BH 886845-67-6
 NTE stereoselective
 RX(26) RCT BH 886845-67-6
 RGT BT 7647-01-0 HCl
 PRO BW 886845-74-5
 SOL 7732-18-5 Water, 67-56-1 MeOH
 CON 3 hours, room temperature
 NTE stereoselective, incremental addition of the reagent

L3 ANSWER 3 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 144:412272 CASREACT [Full-text](#)
 TITLE: A series of 23,24-dihydrodiscodermolide analogues with simplified lactone regions
 AUTHOR(S): Shaw, Simon J.; Sundermann, Kurt F.; Burlingame, Mark A.; Zhang, Dan; Petryka, Joseph; Myles, David C.
 CORPORATE SOURCE: Kosan Biosciences, Inc., Hayward, CA, 94545, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1961-1964
 CODEN: BMCL8; ISSN: 0960-894X
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A collection of seven new 23,24-dihydrodiscodermolide analogs have been synthesized with modifications to the lactone ring, some of which show antiproliferative activities similar to discodermolide.
 REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 119 A + B ==> C...





RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

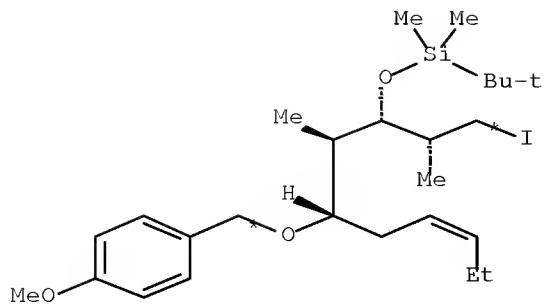
RGF F 7732-18-5 Water

PRO C 884313-57-9

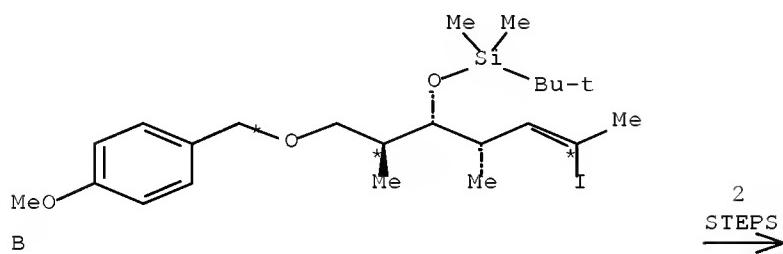
NTE in the dark in stage 2

RX(18) OF 119 COMPOSED OF RX(1), RX(10)

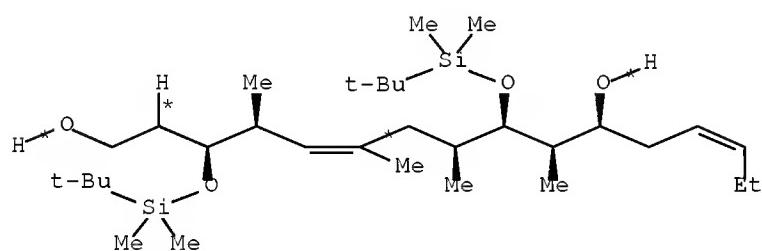
RX(18) A + B ==> AS



A



B



AS
YIELD 63%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 30 minutes, 0 deg C

STAGE(2)

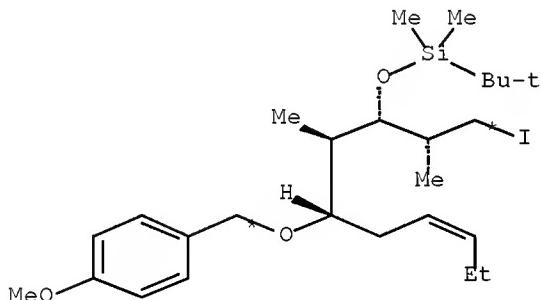
RGT AU 16940-66-2 NaBH₄

SOL 67-56-1 MeOH

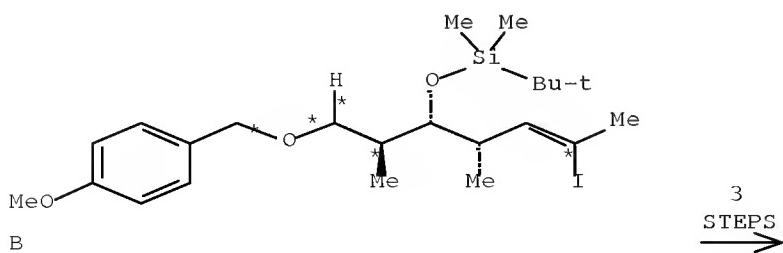
CON 10 minutes

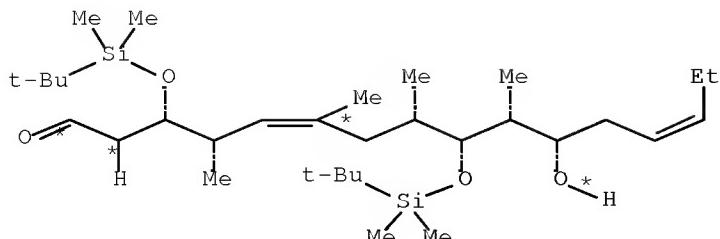
PRO AS 884313-71-7

RX(31) OF 119 COMPOSED OF RX(1), RX(10), RX(11)
 RX(31) A + B ==> AV



A





AV
YIELD 77%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
 NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

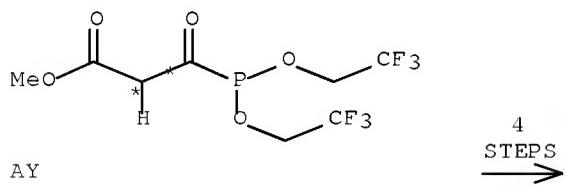
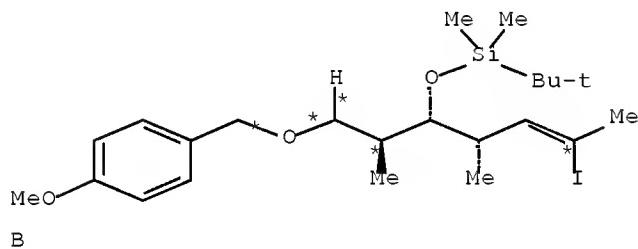
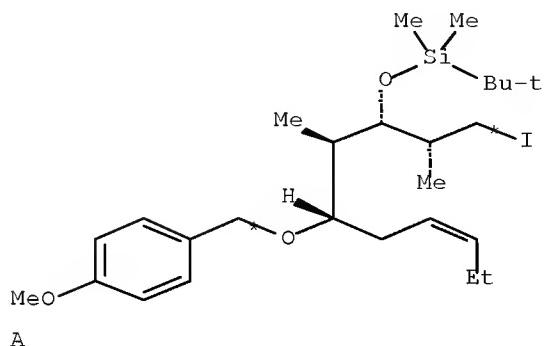
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
 2-iodo-
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

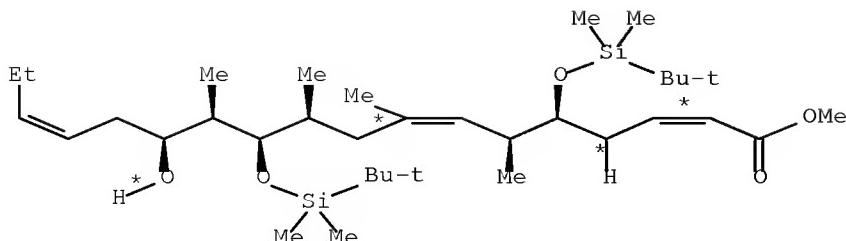
STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
 SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(41) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12)
RX(41) A + B + AY ==> AZ





AZ
YIELD 81%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
 NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
 2-iodo-
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
 SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

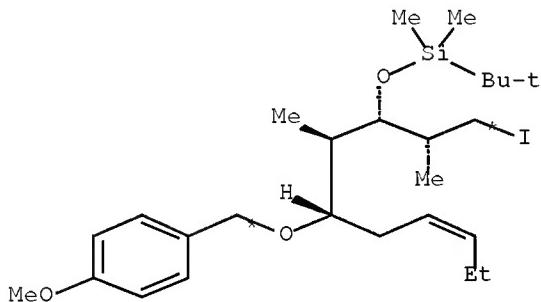
STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

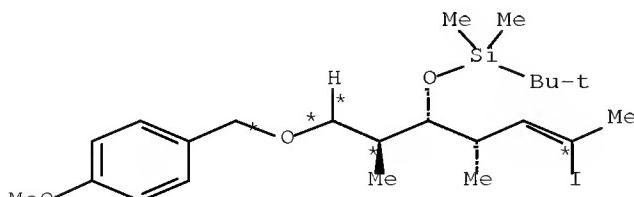
PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

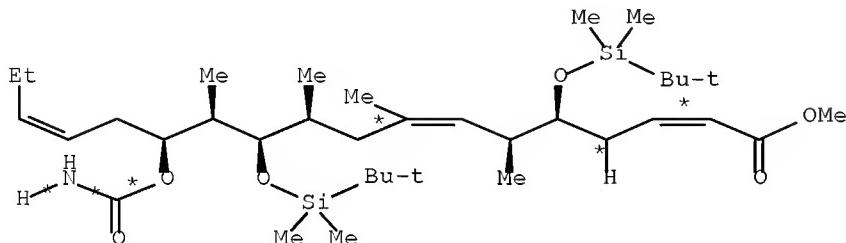
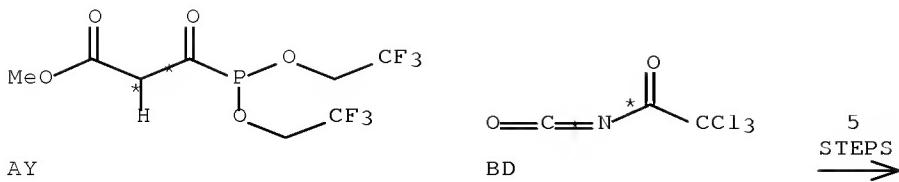
RX(55) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13)
RX(55) A + B + AY + BD ==> BE



A



B



BE
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
 NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
 SOL 67-56-1 MeOH
 CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂C₁₂
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

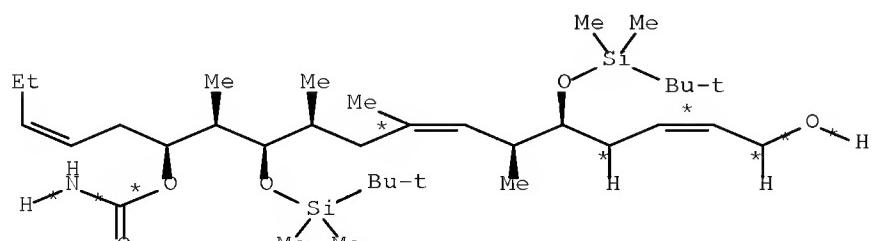
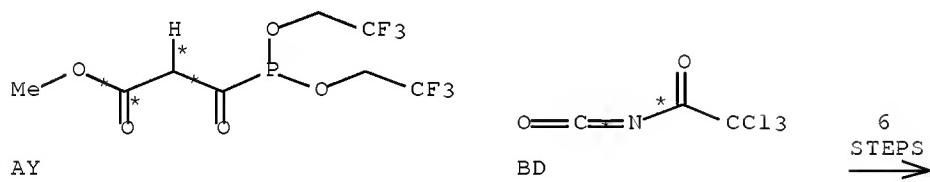
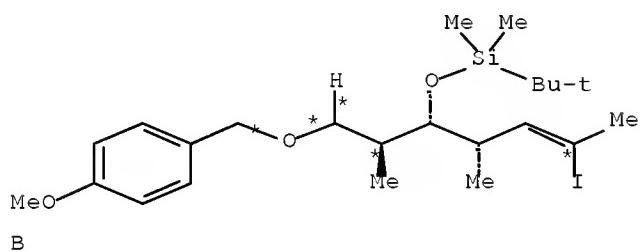
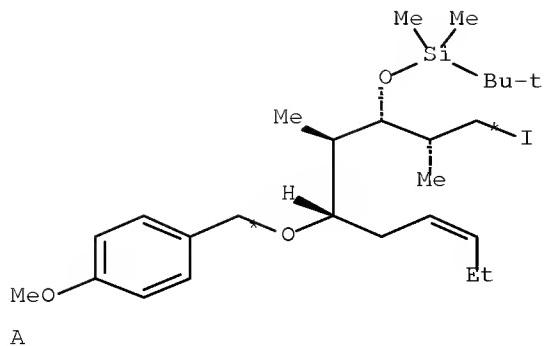
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(78) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14)
RX(78) A + B + AY + BD ==> J



^J
YIELD 88%

RX (1) RCT A 884313-56-8

STAGE(1)
RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)
RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RCT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RCT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

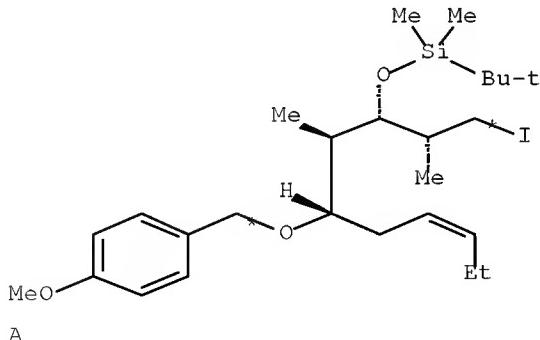
RX(14) RCT BE 884313-74-0

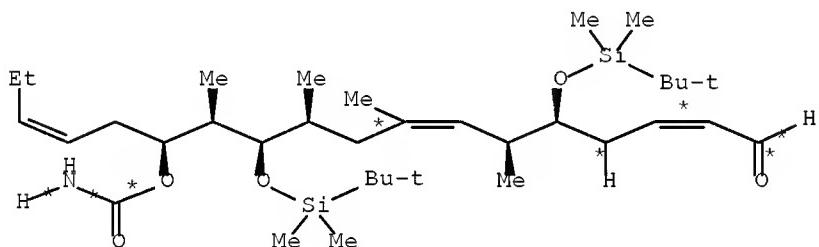
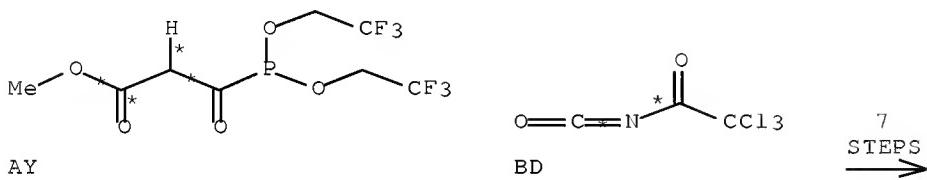
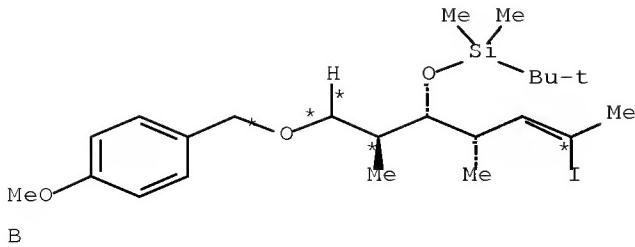
STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(81) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2)
RX(81) A + B + AY + BD ==> K





K
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)

RGF F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

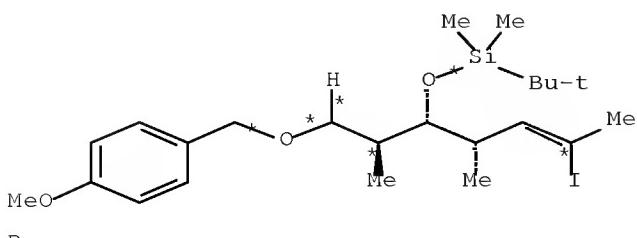
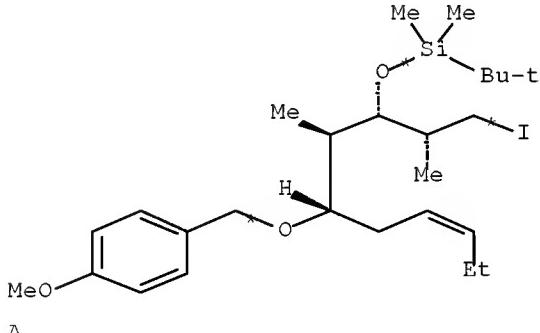
STAGE(2)

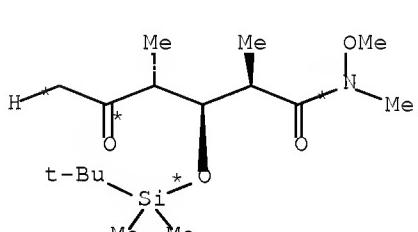
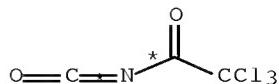
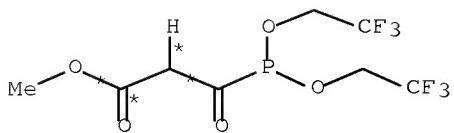
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

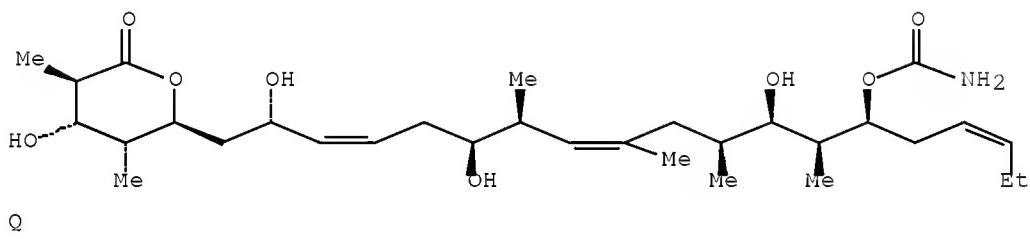
RX(88) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2),
RX(3)

RX(88) A + B + AY + BD + P ==> Q





8
STEPS



RX(1) RCT A 684313-56-8

STAGE (1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE (2)

RCT B 312703-48-5
 CAT 14221-01-3 Pd(PPh3)4
 CON 15 hours, room temperature

STAGE (3)

RGF F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(3) RCT K 884313-58-0, P 397331-43-0

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O

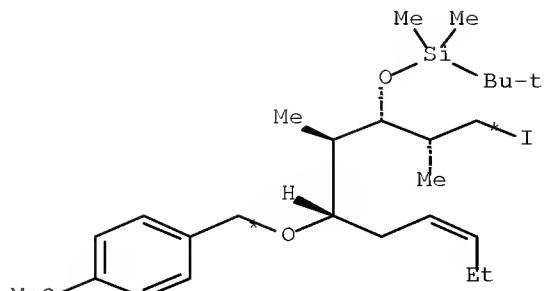
STAGE(2)
RGT T 56553-60-7 Na. (AcO)₃BH

STAGE(3)
RGT U 7647-01-0 HCl
SOL 67-56-1 MeOH

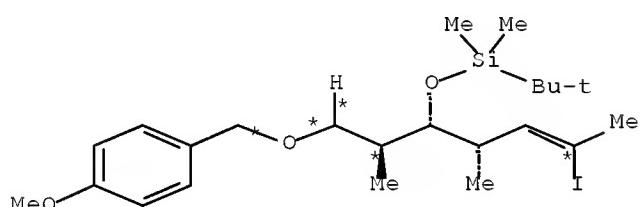
PRO Q 884313-59-1
NTE stereoselective

RX(89) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14), RX(2), RX(15)

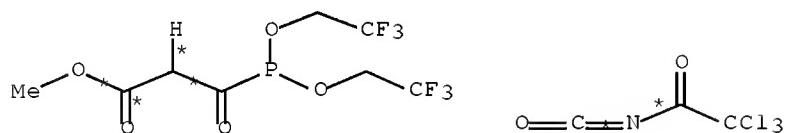
RX(89) A + B + AY + BD + AA ==> BX



A

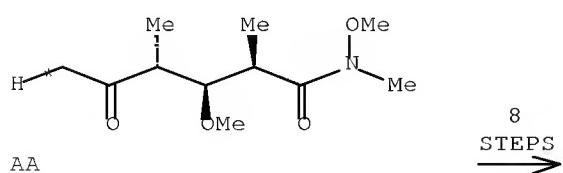


B

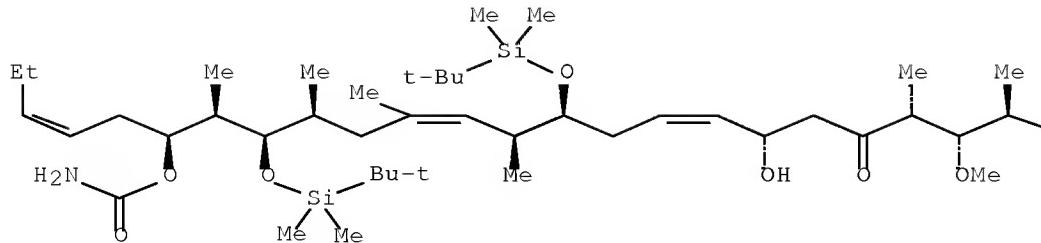


AY

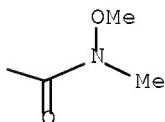
BD



PAGE 1-A



PAGE 1-B



^{BI}
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂C₁₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

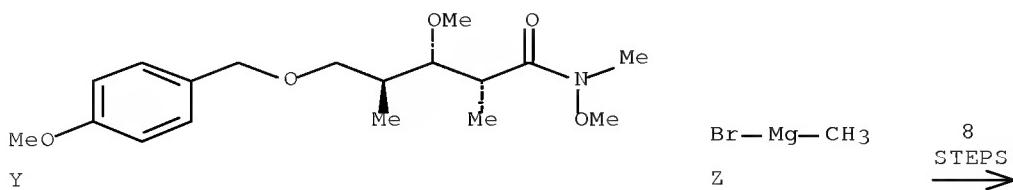
PRO BI 884313-76-2

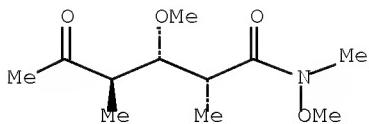
NTE stereoselective, buffered soln. in stage 3

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

RX(99) OF 119 COMPOSED OF REACTION SEQUENCE RX(5), RX(15)
AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15)

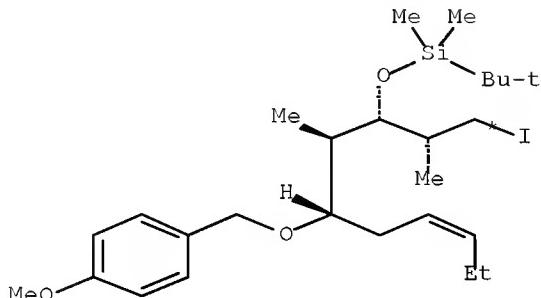
...Y + Z ==> AA...
... A + E + AY + BD + AA ==> BI



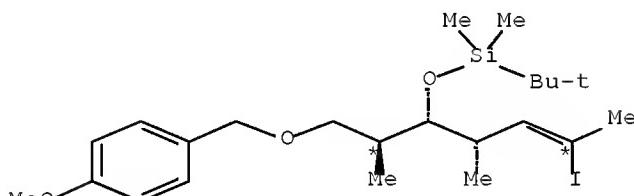


AA

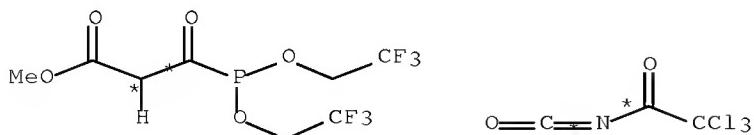
START NEXT REACTION SEQUENCE



A

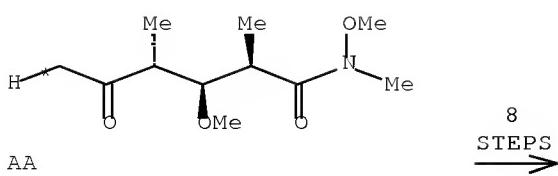


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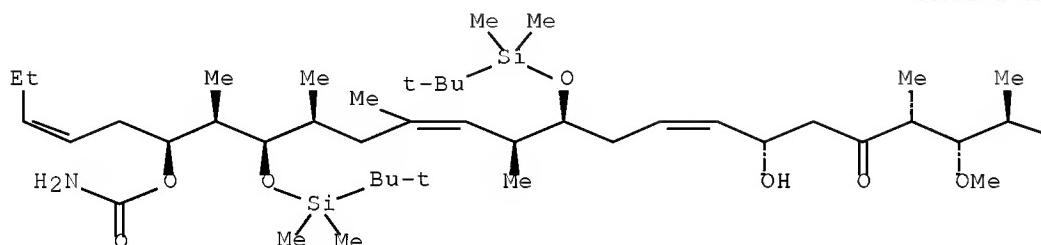


AY

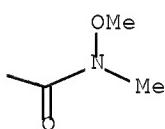
BD



PAGE 1-A



PAGE 1-B



B1
YIELD 87%

RX(5) RCT Y 884313-70-6

STAGE (1)

RGT AB 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂

STAGE (2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE (3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE (1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)
RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)₂
SOL 75-09-2 CH₂Cl₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

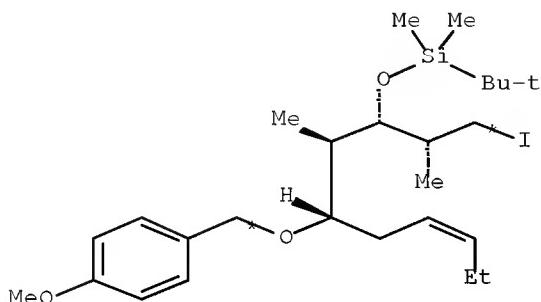
STAGE(3)

RGJ BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

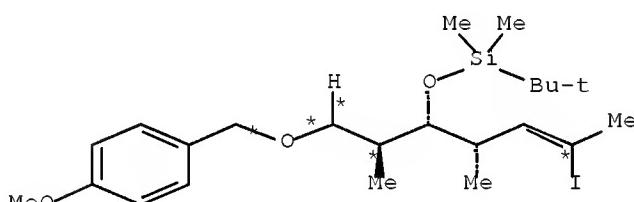
PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

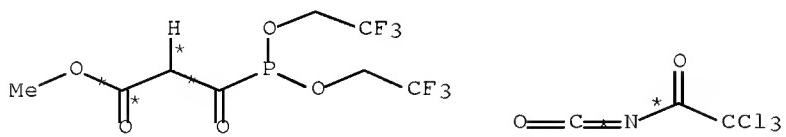
RX(100) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14),
 RX(2), RX(15), RX(16)
 RX(100) A + B + AY + BD + AA ==> W



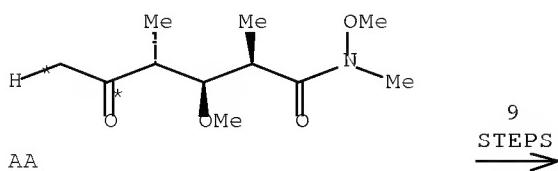
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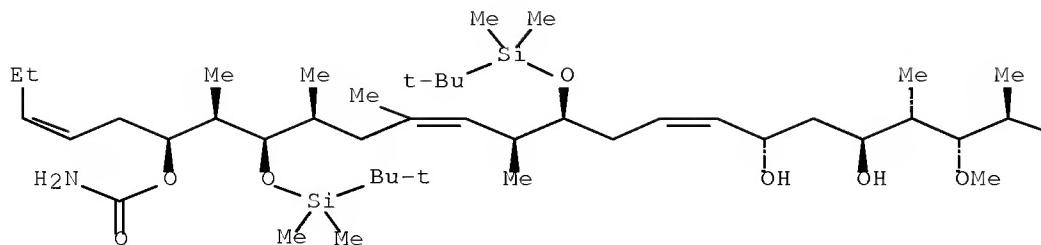
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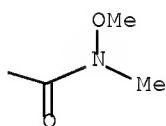
AY



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PAGE 1-B



^W
YIELD 81%

RX(1) RCT A 884313-56-8

STAGE (1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE (2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE (3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE (1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)
RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

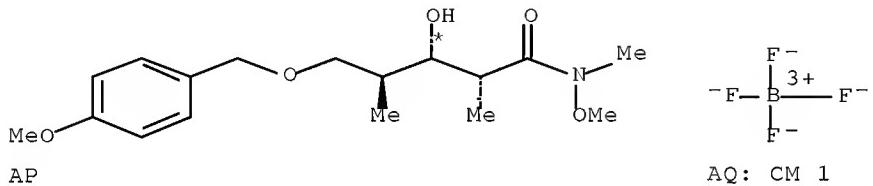
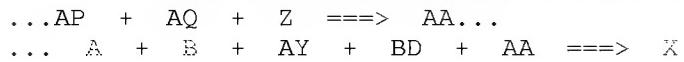
PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

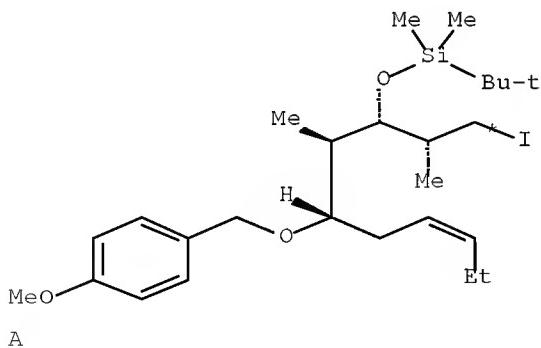
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

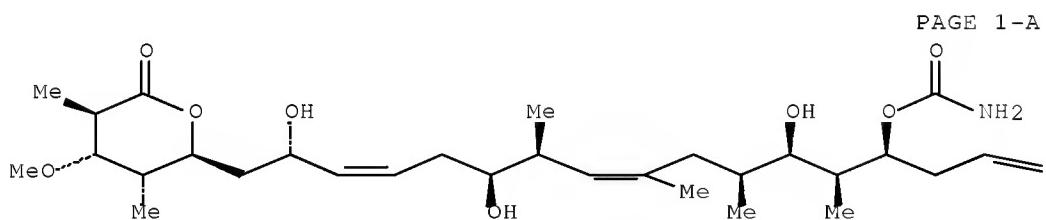
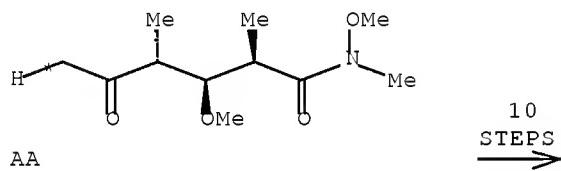
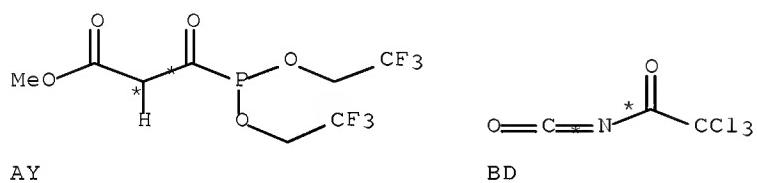
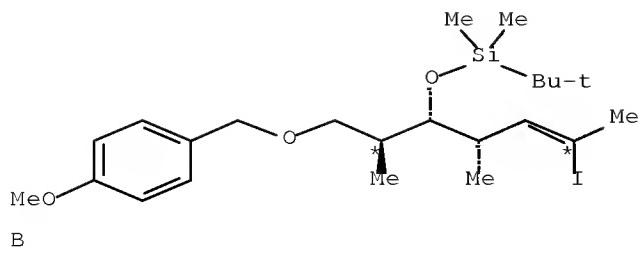
RX(106) OF 119 COMPOSED OF REACTION SEQUENCE RX(9), RX(5), RX(15), RX(16),
RX(4)

AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15), RX(16), RX(4)



START NEXT REACTION SEQUENCE





Et^2

X YIELD 92%

RX(9) RCT AP 252342-49-7, AQ 420-37-1
 RGT AR 20734-58-1 Proton sponge
 PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)
 RGT AB 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂

STAGE(2)
 RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)
 RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)
 RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
 RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)
 RGT F 7732-18-5 Water

PRO C 884313-57-9
 NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
 RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

RX(4) RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature

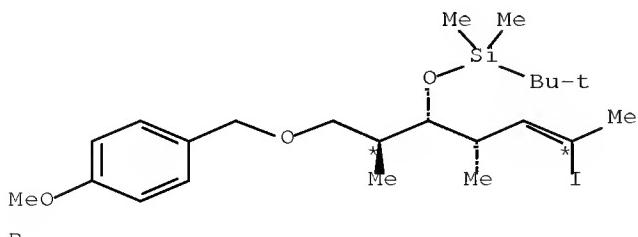
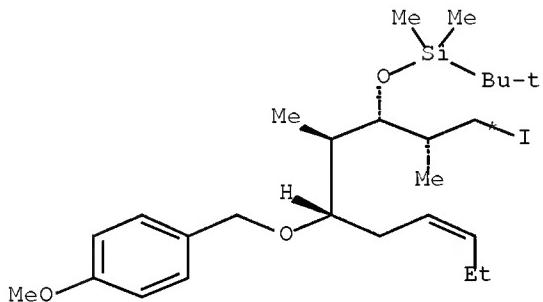
STAGE(2)

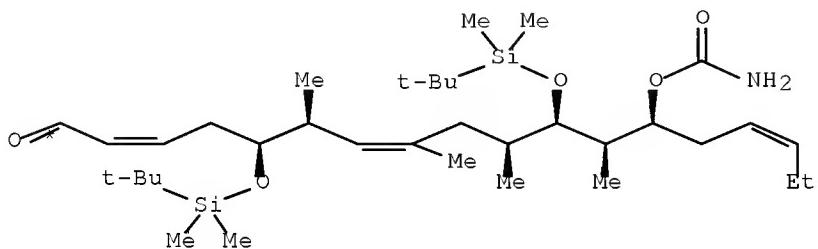
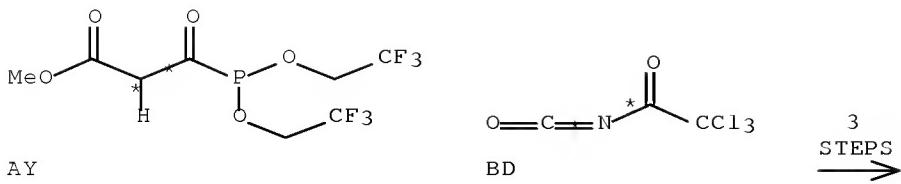
RGT L 144-55-8 NaHCO₃
SOL 75-09-2 CH₂Cl₂
CON neutralized

PRO X 884313-60-4
NTE stereoselective

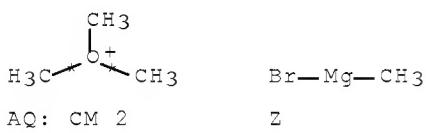
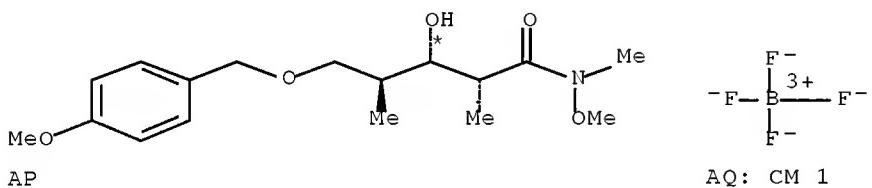
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

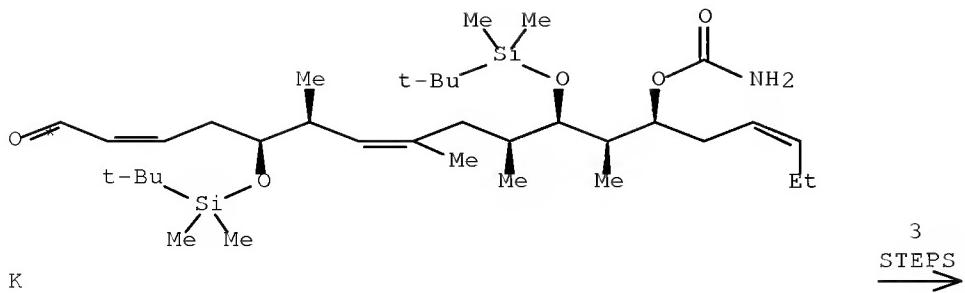
RX(111) OF 119 COMPOSED OF REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12),
RX(13), RX(14), RX(2), RX(15)
AND REACTION SEQUENCE RX(9), RX(5), RX(15)
... A + B + AY + BD ==> K...
...AP + AQ + Z + K ==> BT



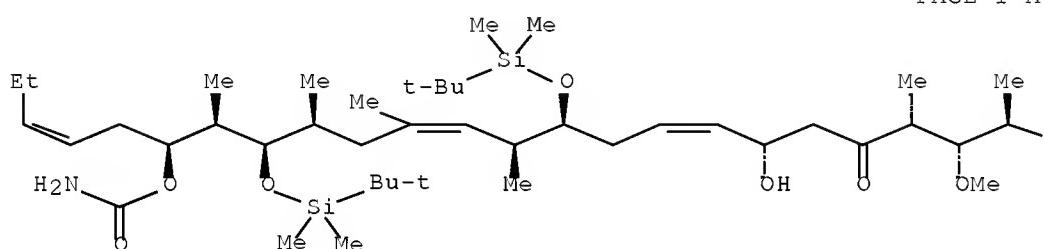


START NEXT REACTION SEQUENCE

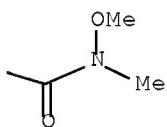




PAGE 1-A



PAGE 1-B



^{BI}
YIELD 87%

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh₃)₄
 CON 15 hours, room temperature

STAGE(3)
RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH

CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(9) RCT AP 252342-49-7, AQ 420-37-1
RGT AR 20734-58-1 Proton sponge
PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)
RGT AB 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂

STAGE(2)
RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)
RCT Z 75-16-1

PRO AA 884313-62-6

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O

CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

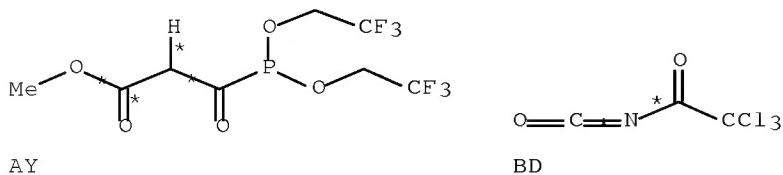
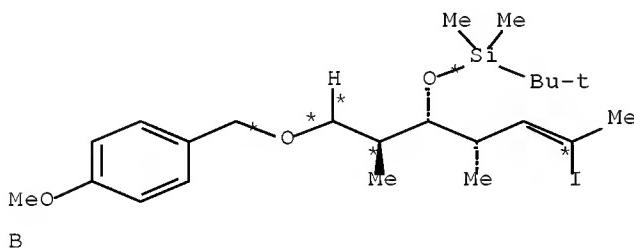
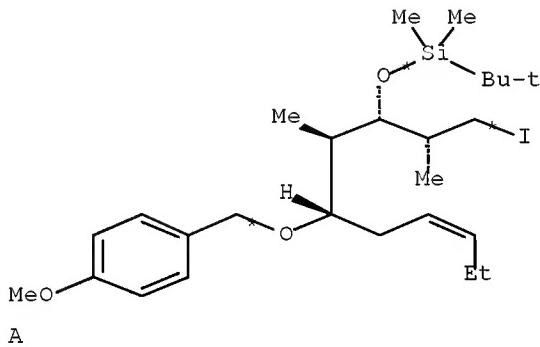
RGT BJ 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

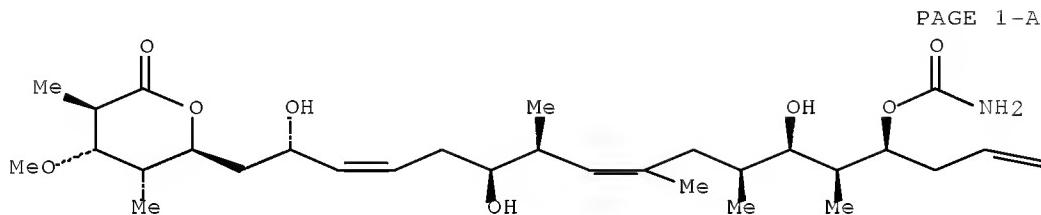
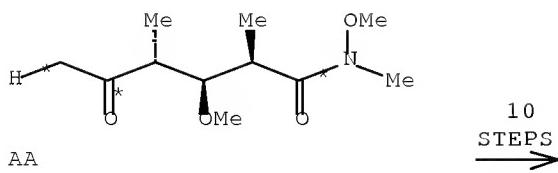
PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(115) OF 119 COMPOSED OF RX(1), RX(10), RX(11), RX(12), RX(13), RX(14),
RX(2), RX(15), RX(16), RX(4)

RX(115) A + B + AY + BD + AA ==> X





PAGE 1-B



X YIELD 92%

RX(1) RCT A 884313-56-8

STAGE (1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
 SOL 60-29-7 Et₂O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE (2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE (3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)

RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)

RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9

NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(2)

RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)

RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)

RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)

RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)

RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)

RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON 5 minutes

PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

RX(4) RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl
 SOL 7732-18-5 Water, 67-56-1 MeOH
 CON 3 hours, room temperature

STAGE(2)

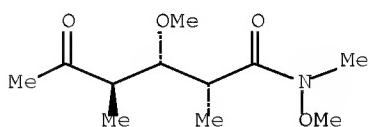
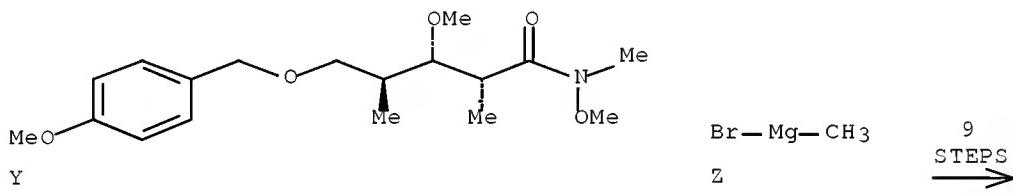
RGT L 144-55-8 NaHCO₃
 SOL 75-09-2 CH₂Cl₂
 CON neutralized

PRO X 884313-60-4

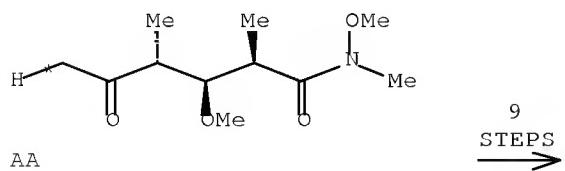
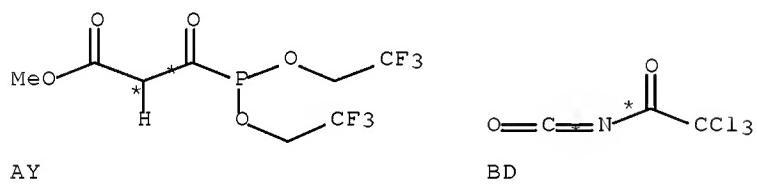
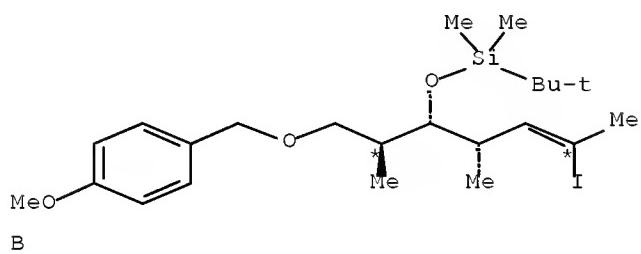
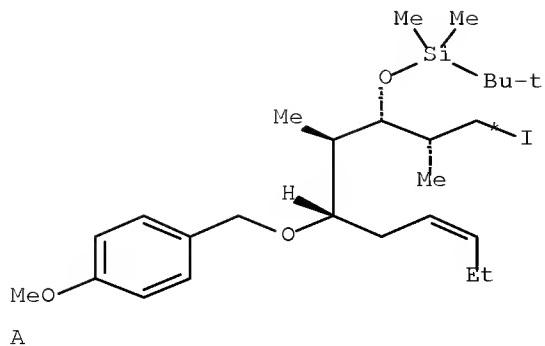
NTE stereoselective

VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

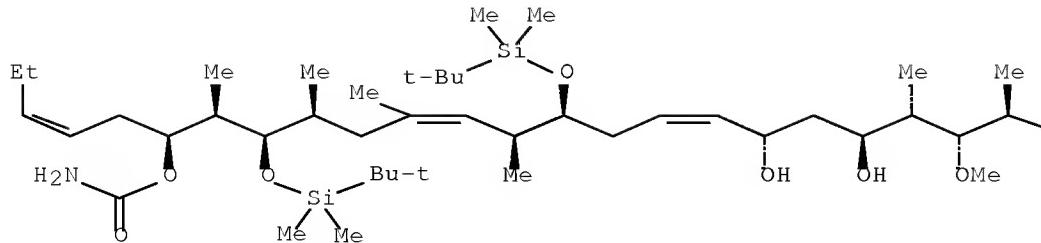
RX(117) OF 119 COMPOSED OF REACTION SEQUENCE RX(5), RX(15), RX(16)
 AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
 RX(14), RX(2), RX(15), RX(16)
 ...Y + Z ==> AA...
 ... A + B + AY + BD + AA ==> W



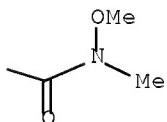
START NEXT REACTION SEQUENCE



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PAGE 1-B



^W
YIELD 81%

RX(5) RCT Y 884313-70-6

STAGE(1)

RGT AB 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et₃N, AD 79-37-8 (COCl)₂

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl₂
SOL 60-29-7 Et₂O, 109-66-0 Pentane
CON SUBSTAGE(1) 0.83 hours, -78 deg C
SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5
CAT 14221-01-3 Pd(PPh₃)₄
CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9
NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
RGT AT 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
CON 30 minutes, 0 deg C

STAGE(2)
RGT AU 16940-66-2 NaBH₄
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me₄-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH₂C₁₂
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K₂CO₃, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K₂CO₃
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH₂C₁₂, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2
NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

STAGE(2)
RCT BI 884313-76-2

SOL 75-05-8 MeCN, 64-19-7 AcOH
 CON SUBSTAGE(1) 0.5 hours, -30 deg C
 SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

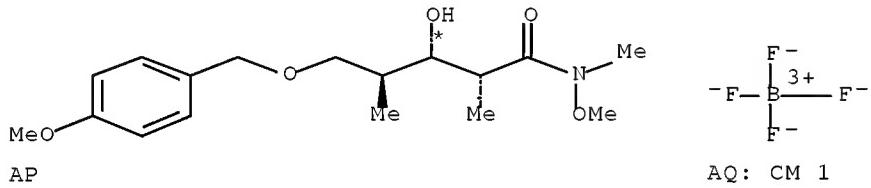
RGT BG 304-59-6 Rochelle salt
 SOL 7732-18-5 Water
 CON 5 minutes

PRO W 984313-78-4

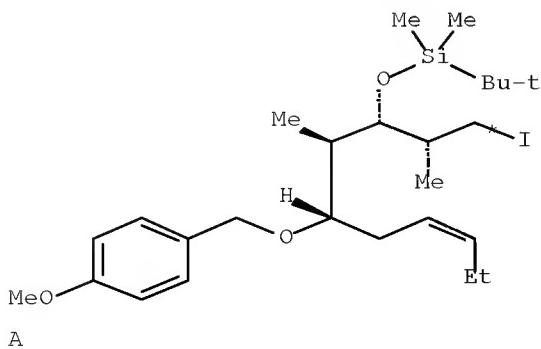
NTE stereoselective, in-situ generated reactant on stage 1

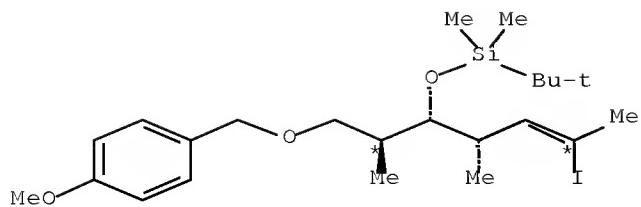
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

RX(118) OF 119 COMPOSED OF REACTION SEQUENCE RX(9), RX(5), RX(15), RX(16)
 AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
 RX(14), RX(2), RX(15), RX(16)
 ...AP + AQ + Z ==> AA...
 ... A + B + AY + BD + AA ==> W

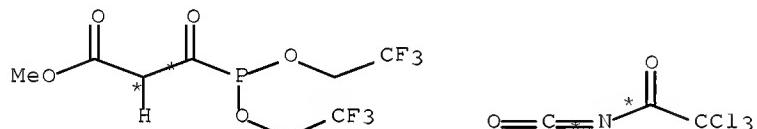


START NEXT REACTION SEQUENCE



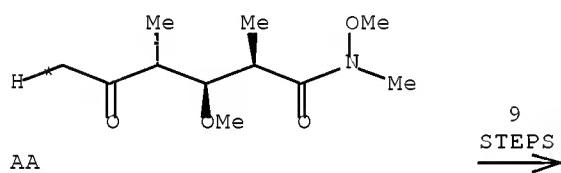


B



A.Y

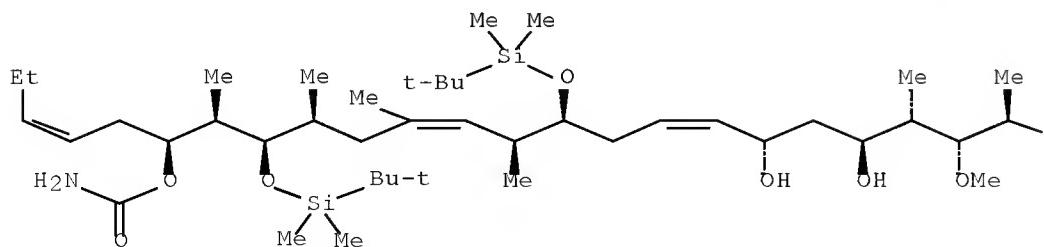
BD

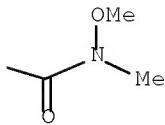


AA

STEPS

PAGE 1-A





^W
YIELD 81%

RX(9) RCT AP 252342-49-7, AQ 420-37-1
 RGT AR 20734-58-1 Proton sponge
 PRO Y 884313-70-6

RX(5) RCT Y 884313-70-6

STAGE(1)
 RGT AB 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2

STAGE(2)
 RGT AC 67-68-5 DMSO, S 121-44-8 Et3N, AD 79-37-8 (COCl)2

STAGE(3)
 RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)
 RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2
 SOL 60-29-7 Et2O, 109-66-0 Pentane
 CON SUBSTAGE(1) 0.83 hours, -78 deg C
 SUBSTAGE(2) 1 hour, room temperature

STAGE(2)
 RCT B 212703-48-5
 CAT 14221-01-3 Pd(PPh3)4
 CON 15 hours, room temperature

STAGE(3)
 RGT F 7732-18-5 Water

PRO C 884313-57-9
 NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)
 RGT AT 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4
SOL 67-56-1 MeOH
CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)
RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3
SOL 7732-18-5 Water

PRO AV 884313-72-8
NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO₃, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂C₁₂
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na₂S₂O₃, L 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et₃N
SOL 60-29-7 Et₂O
CON 1 hour, 0 deg C

STAGE(2)
RCT K 884313-58-0
SOL 60-29-7 Et₂O
CON SUBSTAGE(1) 3 hours, -78 deg C
SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)
RGT BJ 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 0 deg C, pH 7
SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2
NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)
RGT BK 109704-53-2 Me₄N.(AcO)₃BH, BL 64-19-7 AcOH
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON 30 minutes, room temperature

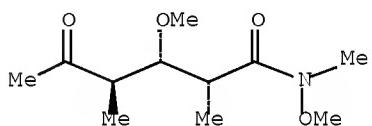
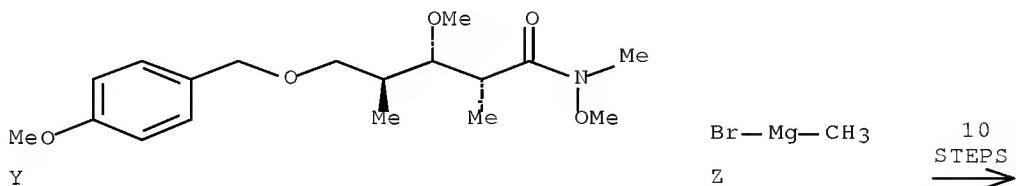
STAGE(2)
RCT BI 884313-76-2
SOL 75-05-8 MeCN, 64-19-7 AcOH
CON SUBSTAGE(1) 0.5 hours, -30 deg C
SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 5 minutes

PRO W 884313-78-4
NTE stereoselective, in-situ generated reactant on stage 1

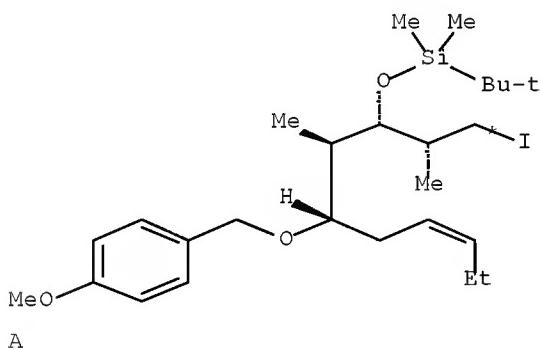
VERIFICATION INCOMPLETE - REACTION MAP DATA UNAVAILABLE

RX(119) OF 119 COMPOSED OF REACTION SEQUENCE RX(5), RX(15), RX(16), RX(4)
AND REACTION SEQUENCE RX(1), RX(10), RX(11), RX(12), RX(13),
RX(14), RX(2), RX(15), RX(16), RX(4)
...Y + Z ==> AA...
... A + B + AY + BD + AA ==> X

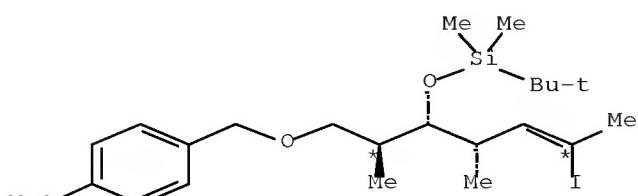


AA

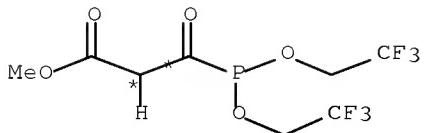
START NEXT REACTION SEQUENCE



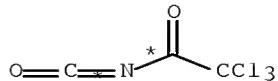
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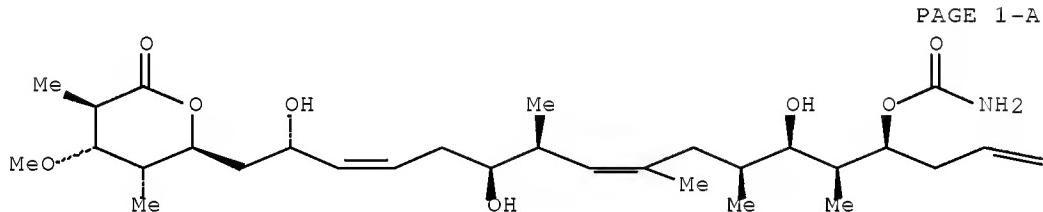
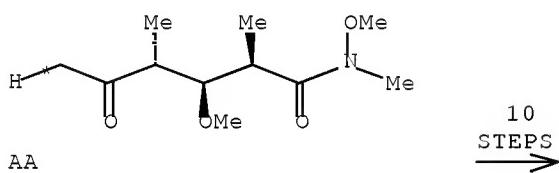
B



AY



BD



PAGE 1-B



^X
YIELD 92%

RX(5) RCT Y 884313-70-6

STAGE (1)
RGT AB 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2

STAGE(2)

RGT AC 67-68-5 DMSO, S 121-44-8 Et3N, AD 79-37-8 (COCl)2

STAGE(3)

RCT Z 75-16-1

PRO AA 884313-62-6

RX(1) RCT A 884313-56-8

STAGE(1)

RGT D 594-19-4 t-BuLi, E 7646-85-7 ZnCl2

SOL 60-29-7 Et2O, 109-66-0 Pentane

CON SUBSTAGE(1) 0.83 hours, -78 deg C

SUBSTAGE(2) 1 hour, room temperature

STAGE(2)

RCT B 212703-48-5

CAT 14221-01-3 Pd(PPh3)4

CON 15 hours, room temperature

STAGE(3)

RGT F 7732-18-5 Water

PRO C 884313-57-9

NTE in the dark in stage 2

RX(10) RCT C 884313-57-9

STAGE(1)

RGT AT 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 30 minutes, 0 deg C

STAGE(2)

RGT AU 16940-66-2 NaBH4

SOL 67-56-1 MeOH

CON 10 minutes

PRO AS 884313-71-7

RX(11) RCT AS 884313-71-7

STAGE(1)

RGT AW 2564-83-2 Me4-piperidoxyl, AX 88-67-5 Benzoic acid,
2-iodo-

SOL 75-09-2 CH2Cl2

CON 2.5 hours, room temperature

STAGE(2)

RGT N 7772-98-7 Na2S2O3

SOL 7732-18-5 Water

PRO AV 884313-72-8

NTE chemoselective, regioselective

RX(12)

STAGE(1)
RGT BA 584-08-7 K2CO3, BB 17455-13-9 18-Crown-6
SOL 108-88-3 PhMe
CON 1 hour, room temperature

STAGE(2)
RCT AV 884313-72-8, AY 884313-77-3
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO AZ 884313-73-9
NTE stereoselective, Still-Gennari reaction

RX(13) RCT AZ 884313-73-9, BD 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
RGT BA 584-08-7 K2CO3
SOL 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 1.5 hours, room temperature

PRO BE 884313-74-0

RX(14) RCT BE 884313-74-0

STAGE(1)
RGT BF 1191-15-7 AlH(Bu-i)2
SOL 75-09-2 CH2Cl2, 110-54-3 Hexane
CON 25 minutes, -78 deg C

STAGE(2)
RGT BG 304-59-6 Rochelle salt
SOL 7732-18-5 Water
CON 1.5 hours, 0 deg C

PRO J 884313-75-1

RX(2) RCT J 884313-75-1

STAGE(1)
RGT L 144-55-8 NaHCO3, M 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 30 minutes, room temperature

STAGE(2)
RGT N 7772-98-7 Na2S2O3, L 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO K 884313-58-0

RX(15) RCT AA 884313-62-6

STAGE(1)
RGT R 112246-73-8 Bicycloheptylborane, S 121-44-8 Et3N
SOL 60-29-7 Et2O

CON 1 hour, 0 deg C

STAGE(2)

RCT K 884313-58-0

SOL 60-29-7 Et2O

CON SUBSTAGE(1) 3 hours, -78 deg C

SUBSTAGE(2) 16 hours, -20 deg C

STAGE(3)

RGT BJ 7722-84-1 H2O2

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 0 deg C, pH 7

SUBSTAGE(2) 1 hour, room temperature

PRO BI 884313-76-2

NTE stereoselective, buffered soln. in stage 3

RX(16)

STAGE(1)

RGT BK 109704-53-2 Me4N.(AcO)3BH, BL 64-19-7 AcOH

SOL 75-05-8 MeCN, 64-19-7 AcOH

CON 30 minutes, room temperature

STAGE(2)

RCT BI 884313-76-2

SOL 75-05-8 MeCN, 64-19-7 AcOH

CON SUBSTAGE(1) 0.5 hours, -30 deg C

SUBSTAGE(2) 1 hour, 0 deg C

STAGE(3)

RGT BG 304-59-6 Rochelle salt

SOL 7732-18-5 Water

CON 5 minutes

PRO W 884313-78-4

NTE stereoselective, in-situ generated reactant on stage 1

RX(4) RCT W 884313-78-4

STAGE(1)

RGT U 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON 3 hours, room temperature

STAGE(2)

RGT L 144-55-8 NaHCO3

SOL 75-09-2 CH2Cl2

CON neutralized

PRO X 884313-60-4

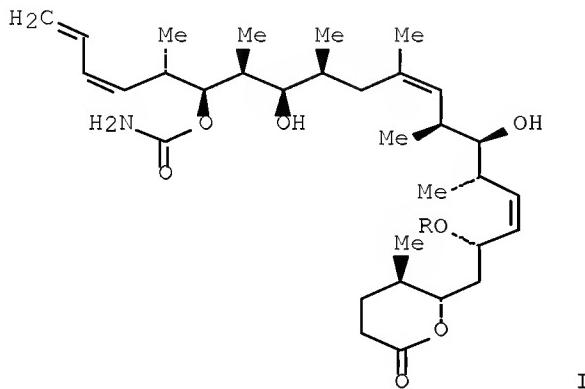
NTE stereoselective

L3 ANSWER 4 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 144:6608 CASREACT Full-text

TITLE: Design, Synthesis, and Biological Evaluation of Simplified Analogues of (+)-Discodermolide. Additional Insights on the Importance of the Diene, the C(7) Hydroxyl, and the Lactone

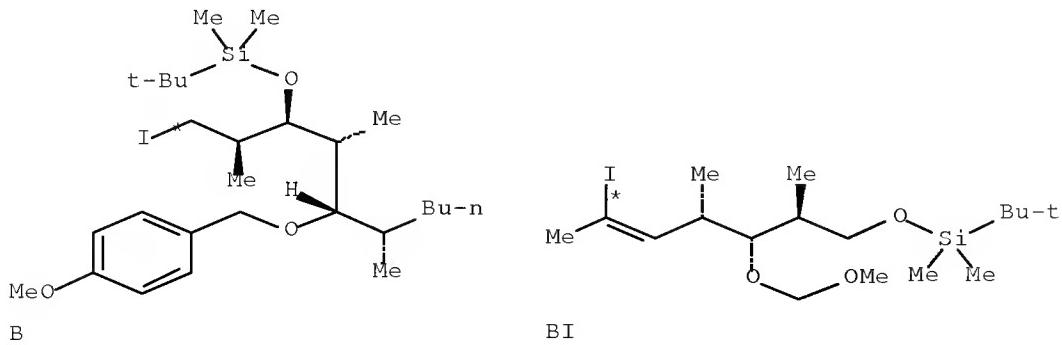
AUTHOR(S): Smith, Amos B., III; Xian, Ming
 CORPORATE SOURCE: Department of Chemistry, Monell Chemical Senses
 Center, and Laboratory for Research on the Structure
 of Matter, University of Pennsylvania, Philadelphia,
 PA, 19104, USA
 SOURCE: Organic Letters (2005), 7(23), 5229-5232
 CODEN: ORLEF7; ISSN: 1523-7060
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



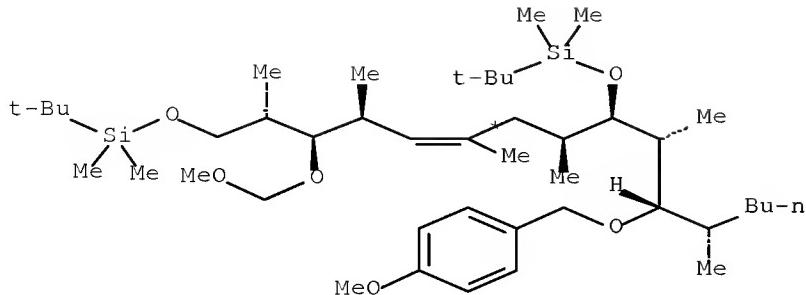
AB The design, synthesis, and biol. evaluation of seven totally synthetic analogs of the antitumor agent (+)-discodermolide are reported. For example, discodermolide analog I ($R = H$) reacted with methoxymethyl chloride to give I ($R = CH_2OMe$) in 40% yield. Saturation of the terminal diene system, alteration of the substituents on the lactone, and alkylation of the C(7)-hydroxyl group reveal significant structure-activity relationships.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(20) OF 268 ...B + BI ==> BJ...



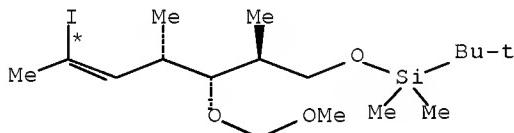
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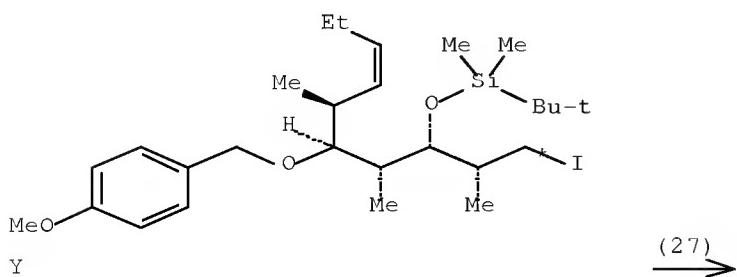
BJ
YIELD 82%

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs₂CO₃
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

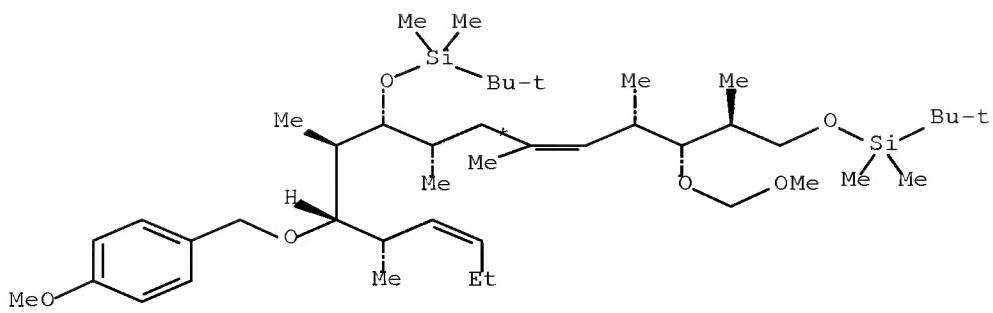
RX(27) OF 268 ...BI + Y ==> BV...



BI



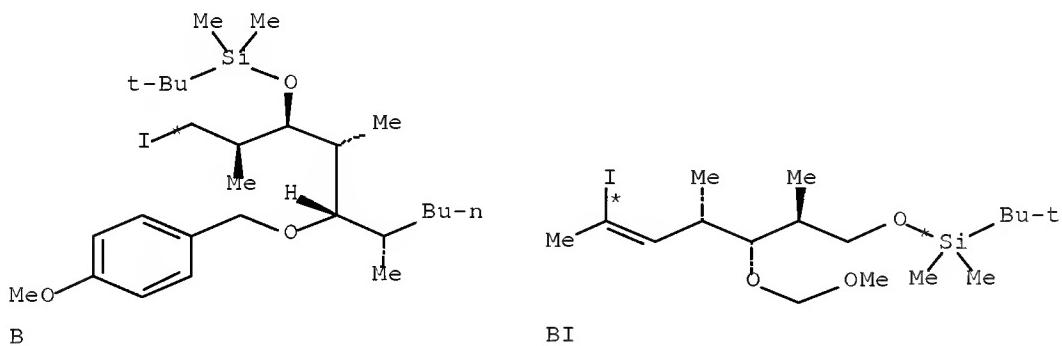
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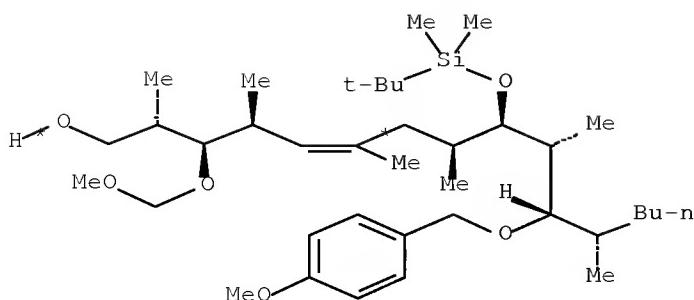
BV
YIELD 85%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(55) OF 268 COMPOSED OF RX(20), RX(21)
RX(55) $\stackrel{\text{min}}{\longrightarrow}$ + $\stackrel{\text{BT}}{\longrightarrow}$ ==> I



2
STEPS
→

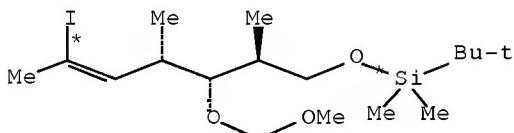


I
YIELD 90%

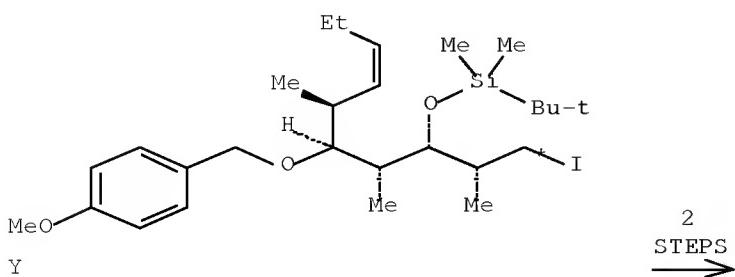
RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

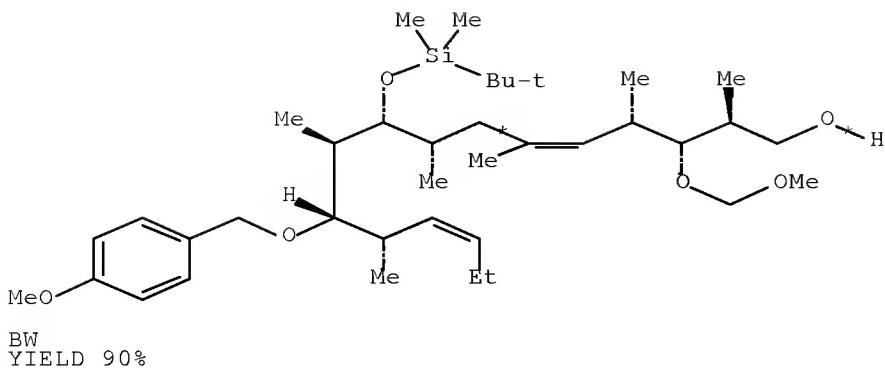
RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(62) OF 268 COMPOSED OF RX(27), RX(28)
 RX(62) BI + Y ==> BW



BI

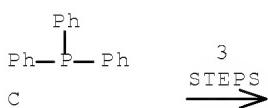
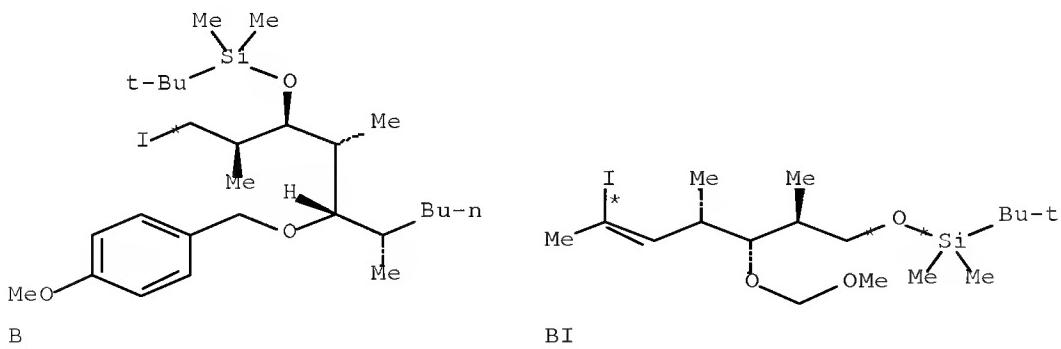


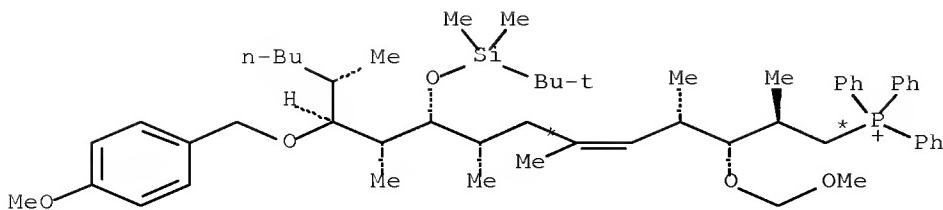


RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(104) OF 268 COMPOSED OF RX(20), RX(21), RX(2)
 RX(104) B + BI + C ==> J





● I⁻

^J
YIELD 89%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

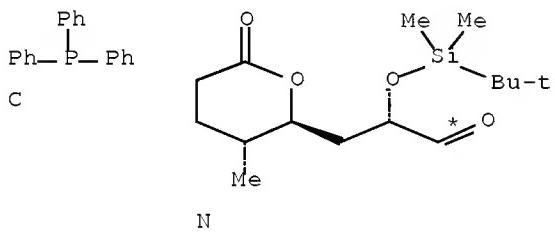
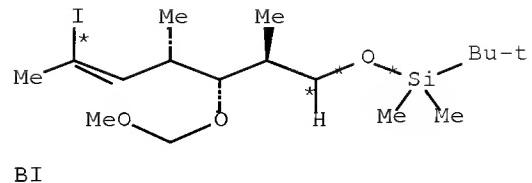
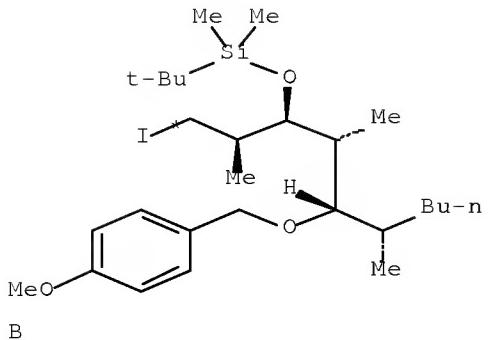
RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

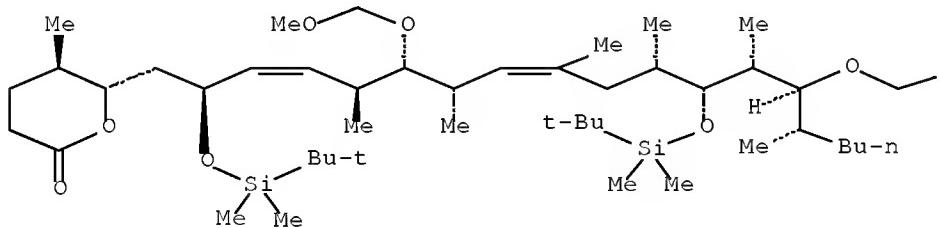
PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(107) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23)
 RX(107) E + BI + C + N ==> R

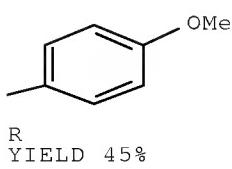


4
STEPS

PAGE 1-A



PAGE 1-B



RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃

PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

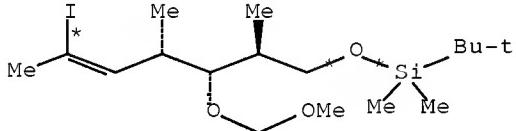
STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

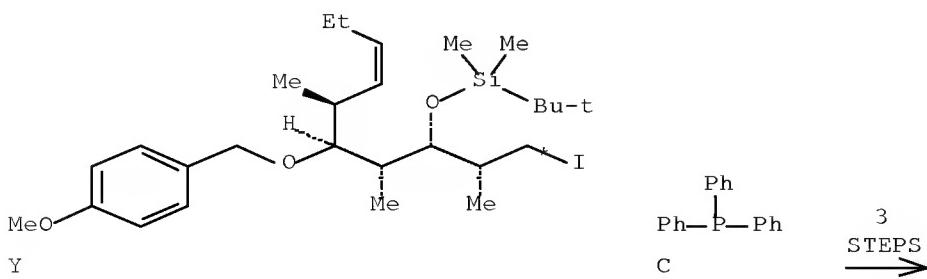
PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

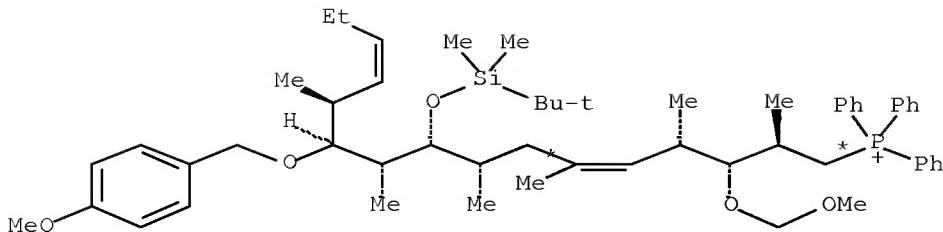
RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(116) OF 268 COMPOSED OF RX(27), RX(28), RX(29)
 RX(116) BI + Y + C ==> BX



BI





● I⁻

BX
YIELD 85%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

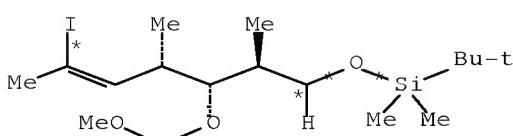
RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

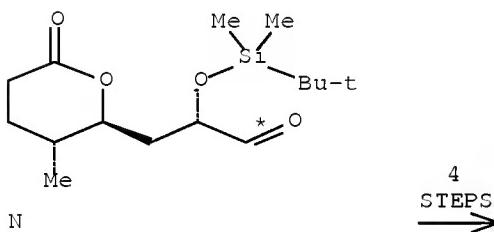
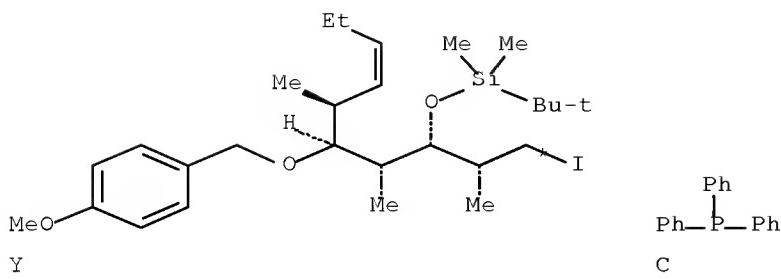
STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(119) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30)
 RX(119) BI + Y + C + N ==> BY

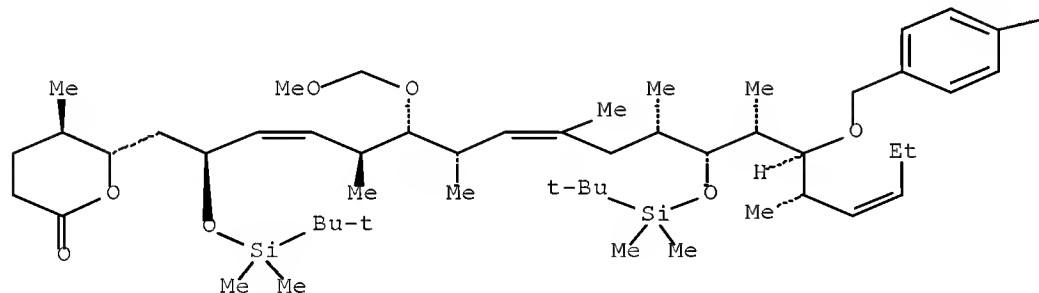


BI



4
STEPS
→

PAGE 1-A



PAGE 1-B

OMe

BY
YIELD 50%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs₂CO₃

PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE (1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

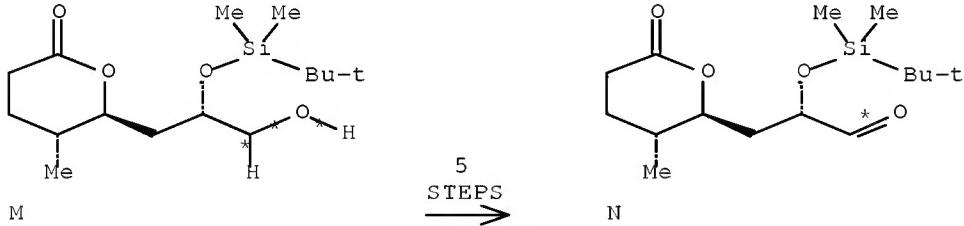
STAGE (2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

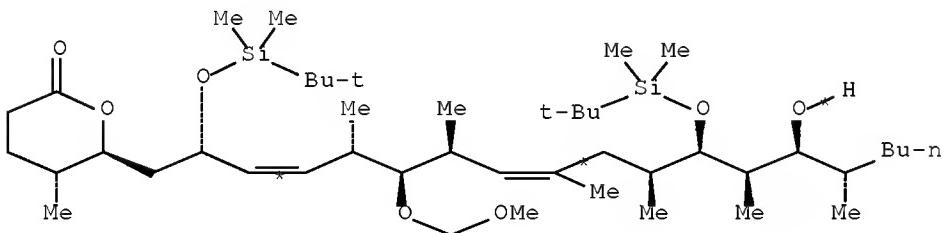
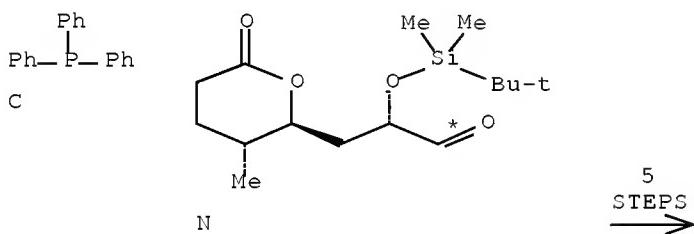
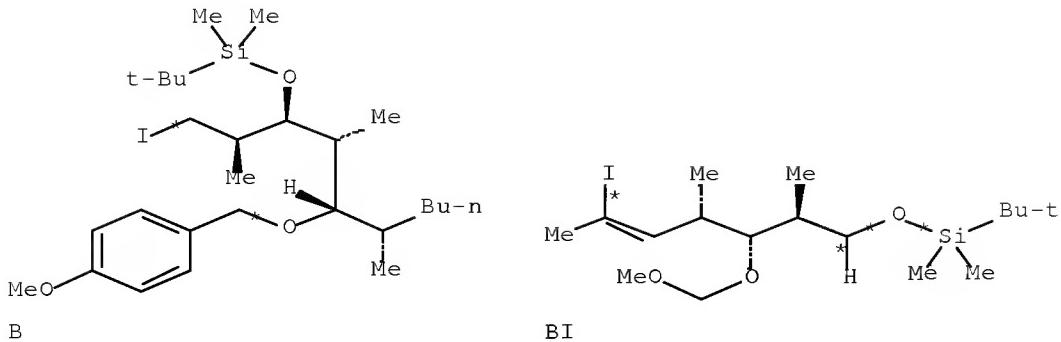
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcoEt
 NTE Wittig coupling

RX(151) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4)

...M ==> N...
 ... B + BI + C + N ==> S



START NEXT REACTION SEQUENCE



S
YIELD 80%

RX(3) RCT M 870075-20-0

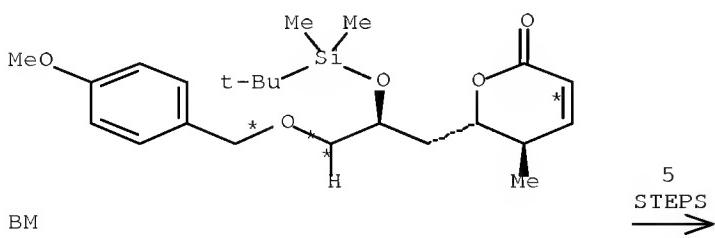
STAGE(1)

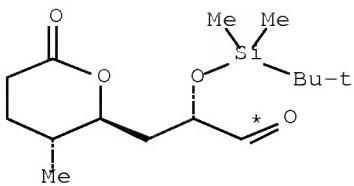
RG_T E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂C₁₂
 CON 2.5 hours, room temperature

STAGE(2)

RG_T P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

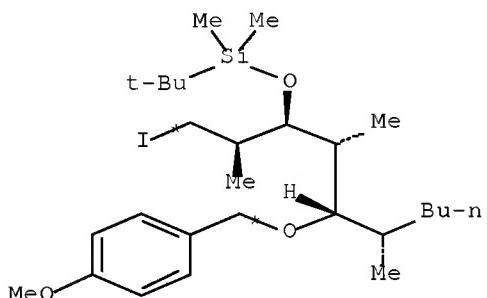
PRO N 853055-22-8
 RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling
 RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water
 RX(2) RCT I 870075-19-7
 STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole
 STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C
 PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%
 RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling
 RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%
 RX(152) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4)
 ...BM ==> N...
 ... B + BI + C + N ==> S



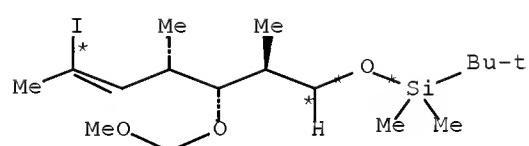


N

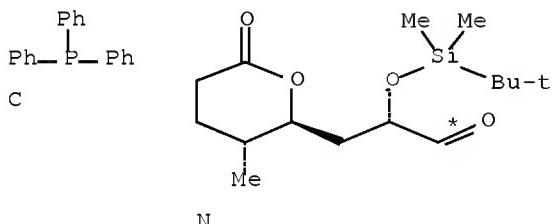
START NEXT REACTION SEQUENCE



B



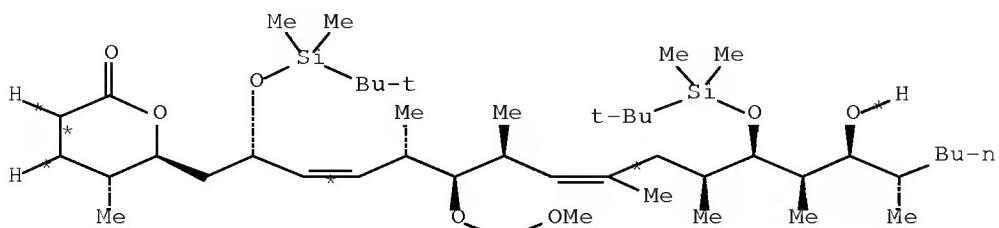
BI



C

N

5 STEPS
→



^S
YIELD 80%

RX(22) RCT BM 837383-29-6
RGT AU 1333-74-0 H2
PRO M 870075-20-0
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs2CO3
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

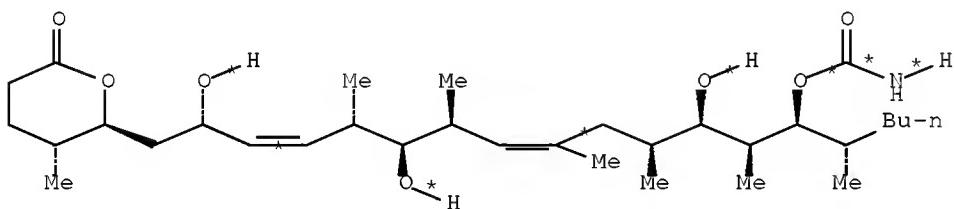
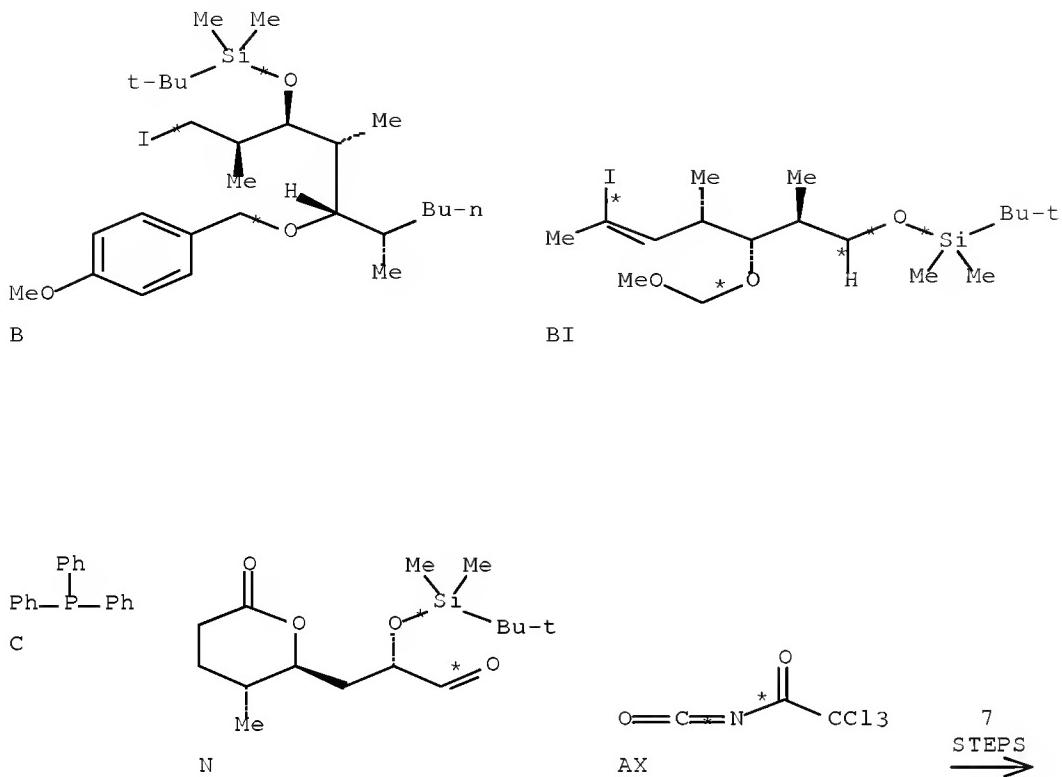
PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

RX(153) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4), RX(24), RX(5)

RX(153) B + BI + C + N + AX ==> V



V YIELD 63%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et3N

CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

PRO R 870075-21-1

NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1

RGT T 84-58-2 DDQ

PRO S 870075-00-6

NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4

PRO U 870075-22-2

NTE literature preparation

RX(5) RCT U 870075-22-2

RGT W 7647-01-0 HCl

PRO V 870075-01-7

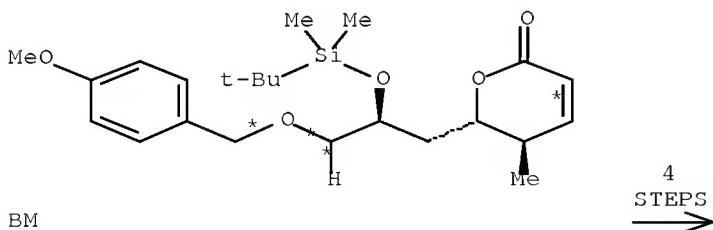
SOL 7732-18-5 Water

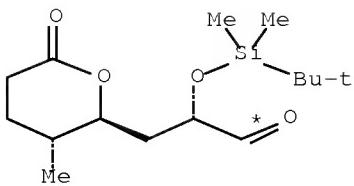
NTE yield over 2 steps = 54%

RX(154) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23)
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23)

...BM ==> N...

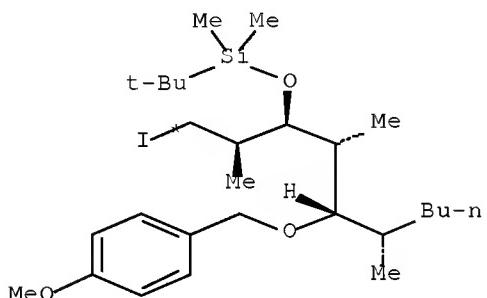
... B + BI + C + N ==> R



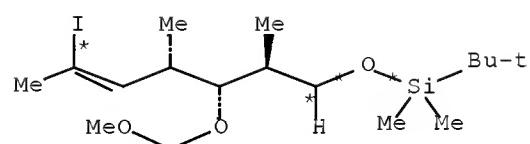


N

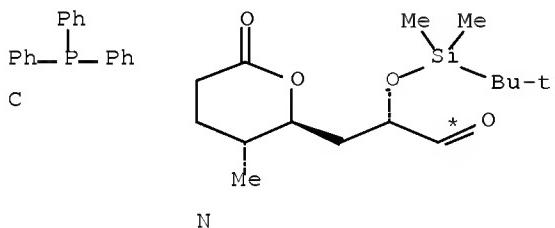
START NEXT REACTION SEQUENCE



B



BI

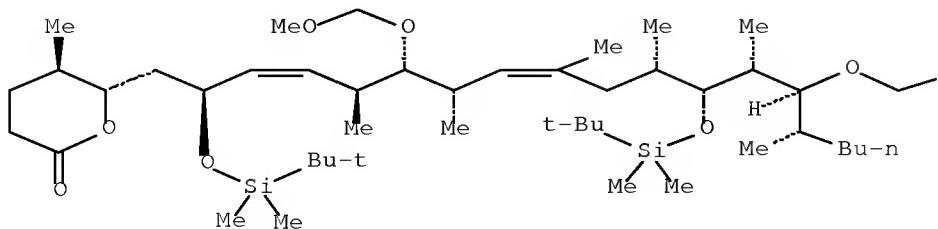


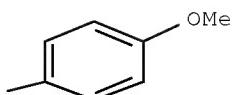
C

N

4 STEPS
→

PAGE 1-A





R
YIELD 45%

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H₂
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE (1)
 RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE (2)
 RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE (1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

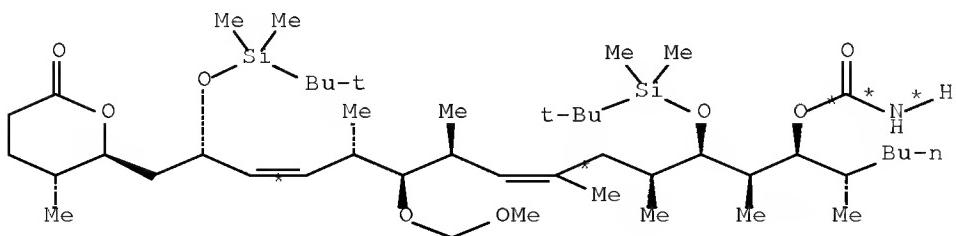
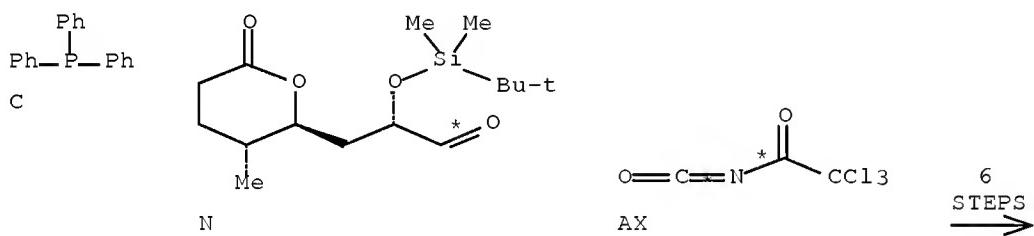
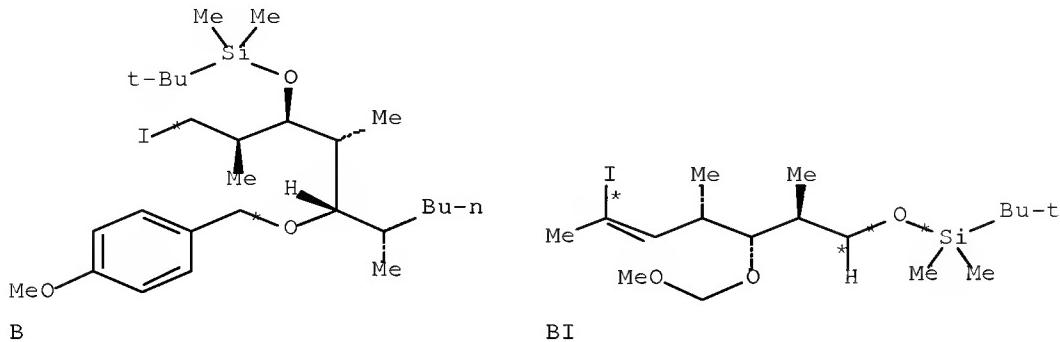
STAGE (2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi

PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

RX(155) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4), RX(24)
 RX(155) B + BI + C + N + AX ==> U



YIELD 85%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-

κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO J 870074-99-0
 NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
 RGT AI 917-54-4 MeLi
 PRO R 870075-21-1
 NTE stereoselective, Wittig coupling

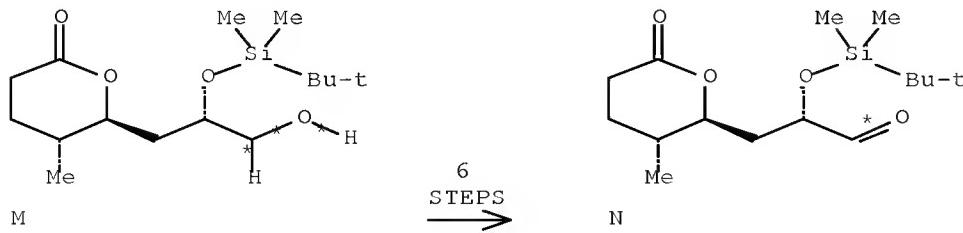
RX(4) RCT R 870075-21-1
 RGT T 84-58-2 DDQ
 PRO S 870075-00-6
 NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4
 PRO U 870075-22-2
 NTE literature preparation

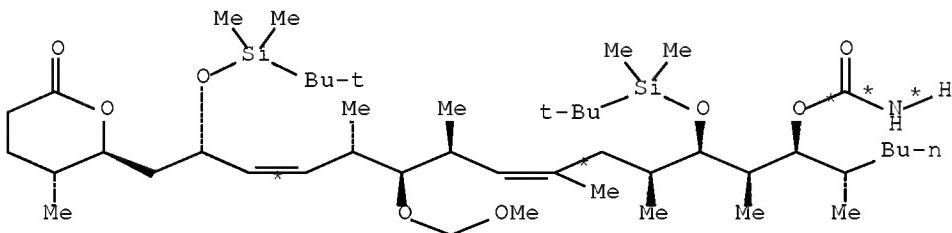
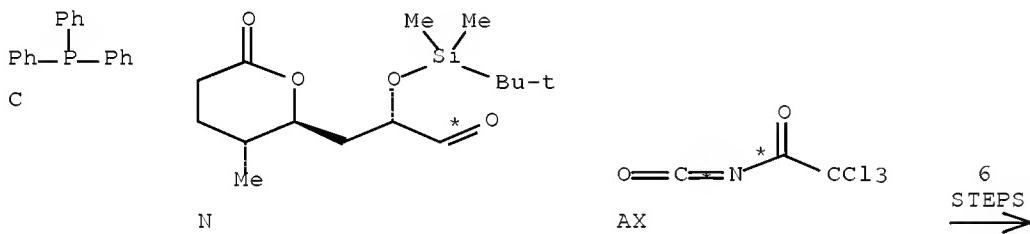
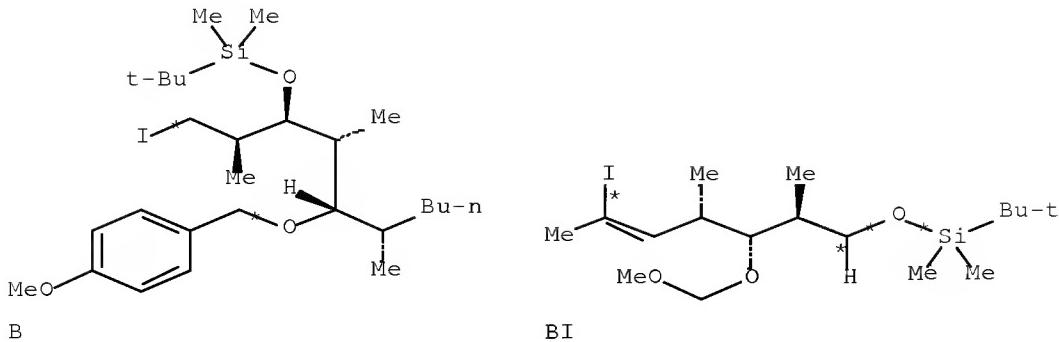
RX(156) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4), RX(24)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),

RX(24)

...M ==> N...
 ... E + BI + C + N + AX ==> Y



START NEXT REACTION SEQUENCE



RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs₂CO₃
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et₃N
CON 100 deg C

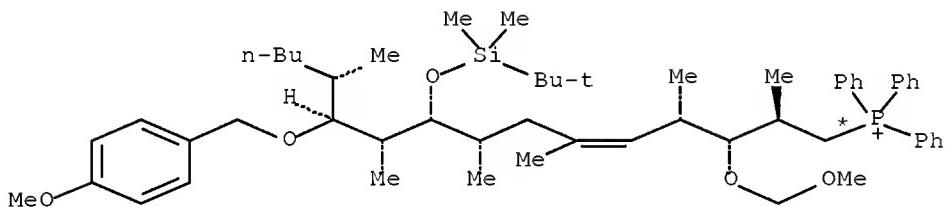
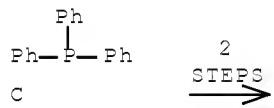
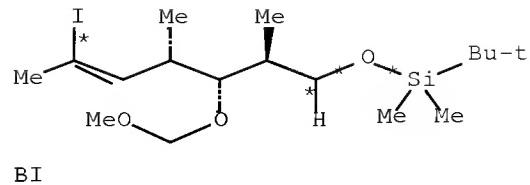
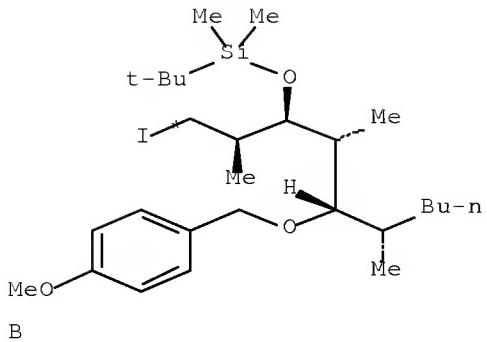
PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4
PRO U 870075-22-2
NTE literature preparation

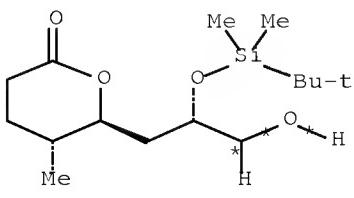
RX(164) OF 268 COMPOSED OF REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23)
AND REACTION SEQUENCE RX(3), RX(23)
... B + BI + C ==> J...
...M + J ==> R

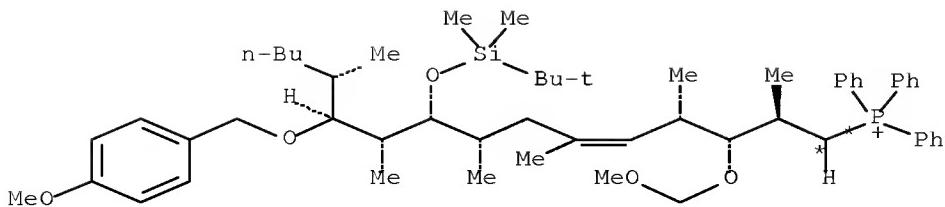


● I⁻

J

START NEXT REACTION SEQUENCE



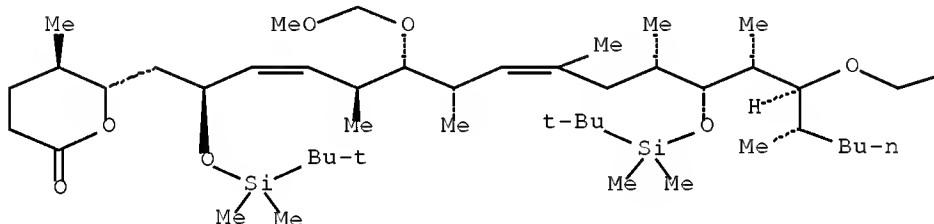


● I⁻

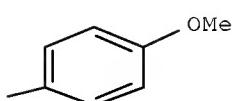
J

2
STEPS
→

PAGE 1-A



PAGE 1-B



R
YIELD 45%

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6

RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

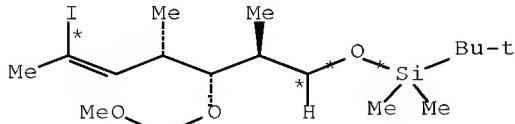
STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

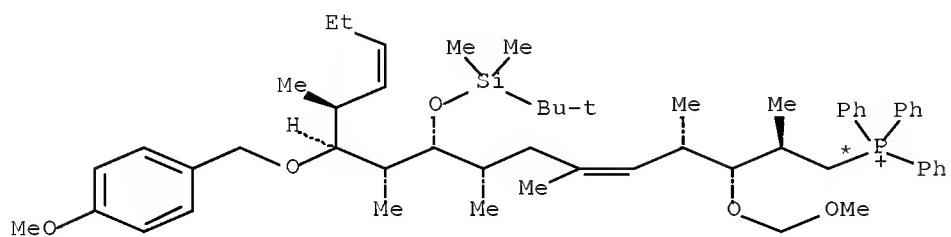
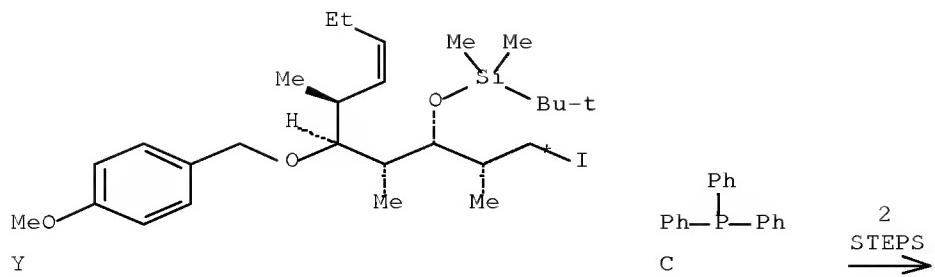
RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

RX(165) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30)
AND REACTION SEQUENCE RX(3), RX(30)

... BI + Y + C ==> BX...
...M + BX ==> BY



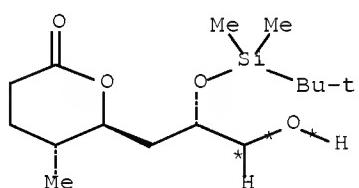
BI

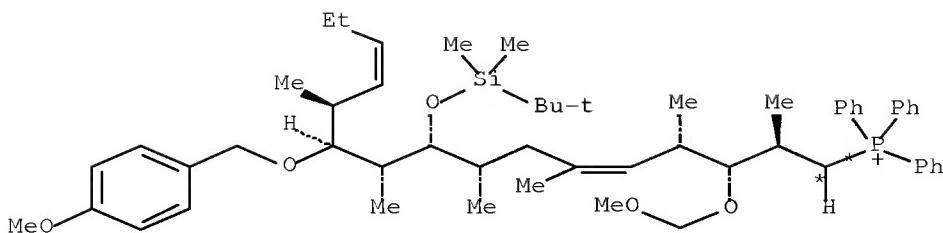


$\bullet \text{I}^-$

BX

START NEXT REACTION SEQUENCE



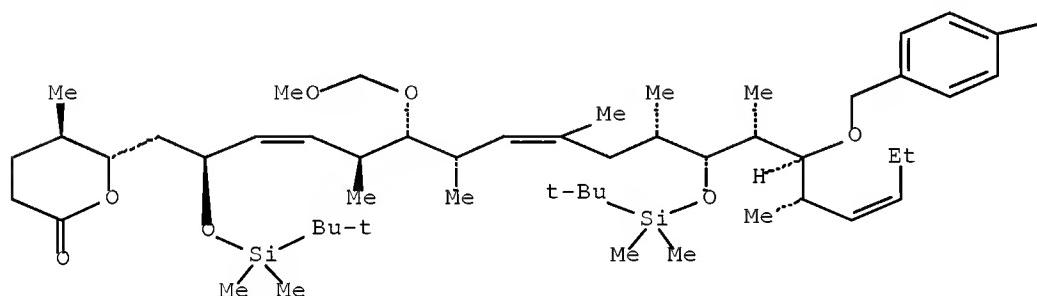


● I-

BX

$\xrightarrow[2]{\text{STEPS}}$

PAGE 1-A



PAGE 1-B

—OMe

BY
YIELD 50%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

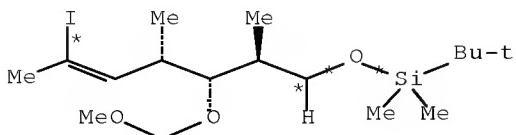
STAGE(2)
 RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

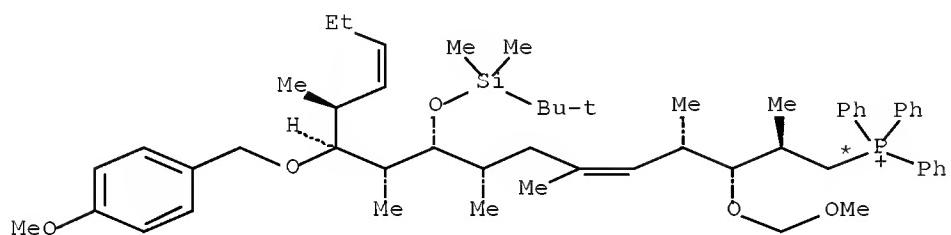
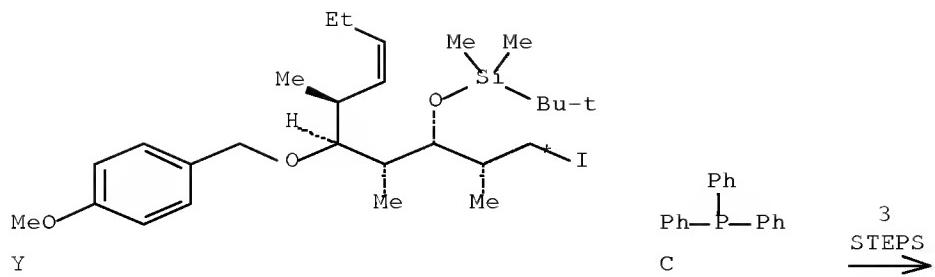
PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

RX(174) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30)
 AND REACTION SEQUENCE RX(22), RX(3), RX(30)

... BI + Y + C ==> BX...
 ...BM + BX ==> BY

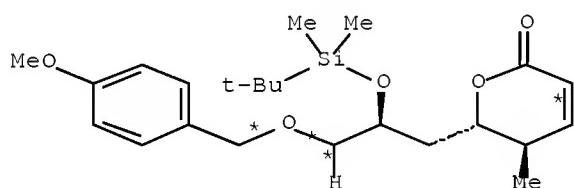




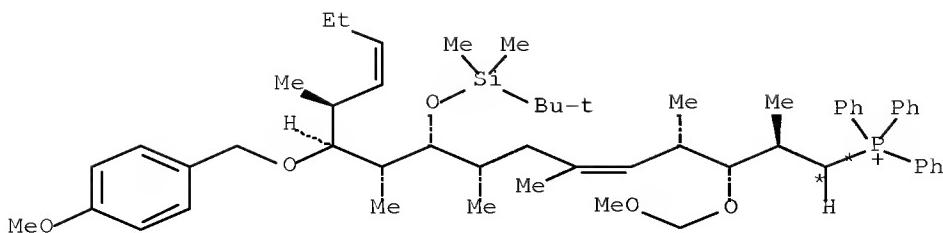
● I⁻

BX

START NEXT REACTION SEQUENCE



BM

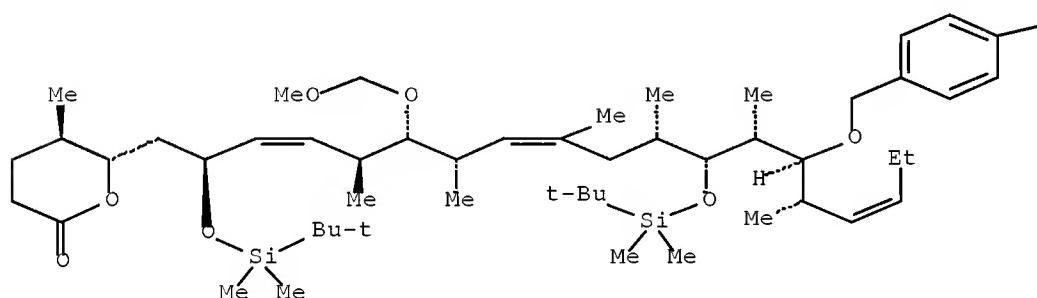


● I-

BX

³
STEPS
→

PAGE 1-A



PAGE 1-B

—OMe

BY
YIELD 50%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
RGT AU 1333-74-0 H2
PRO M 870075-20-0
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

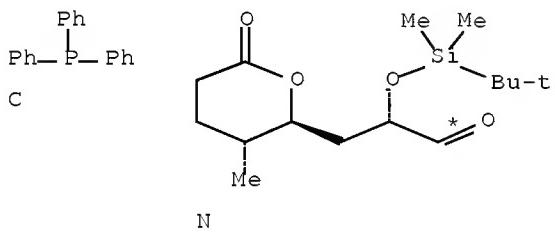
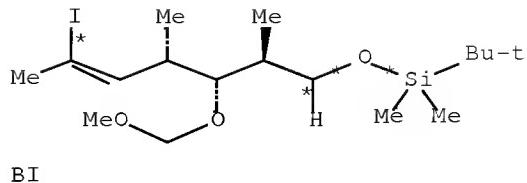
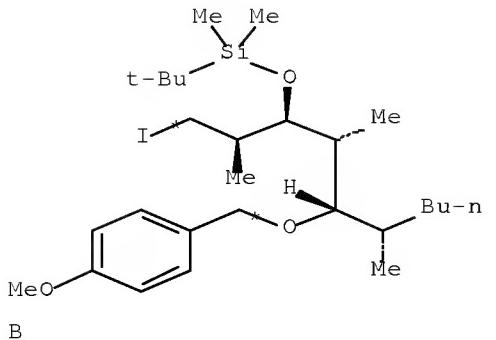
STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2C12
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

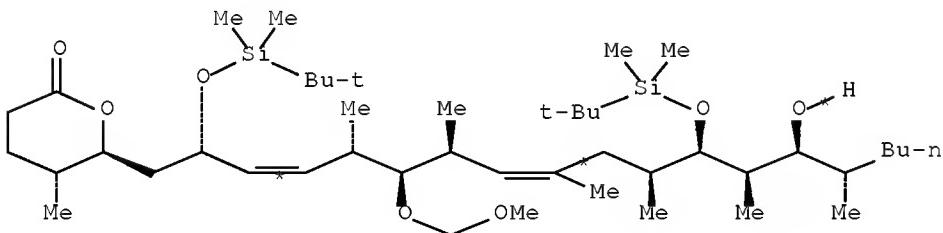
PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H2
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt
NTE Wittig coupling

RX(190) OF 268 COMPOSED OF RX(20), RX(21), RX(2), RX(23), RX(4)
RX(190) B + BI + C + N ==> S



5
STEPS
→



S
YIELD 80%

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs₂CO₃
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE (1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE (2)

RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

PRO R 870075-21-1

NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1

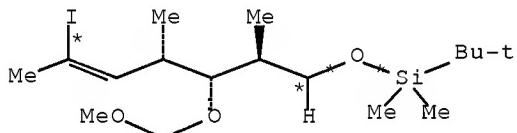
RGT T 84-58-2 DDQ

PRO S 870075-00-6

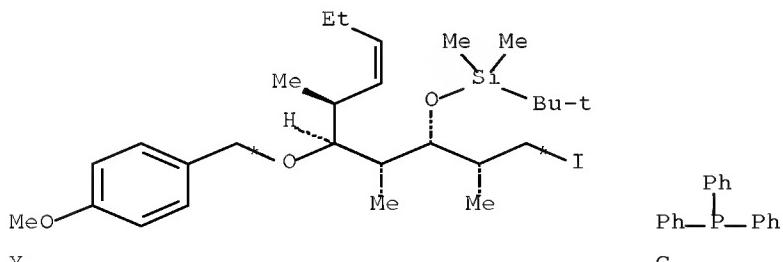
NTE yield over 2 steps = 36%

RX(201) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31)

RX(201) BI + Y + C + N ==> BZ

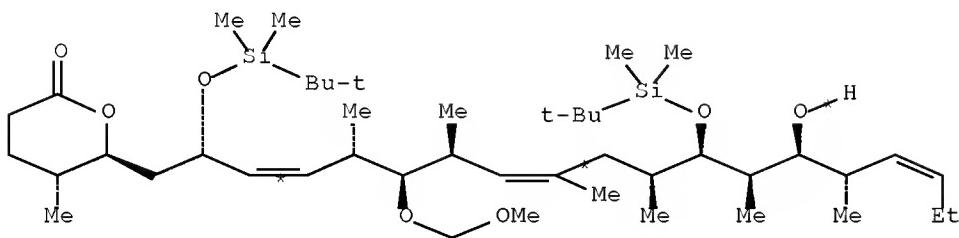
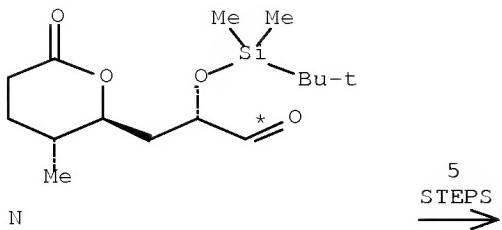


BI



Y

C



BZ
YIELD 93%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RGT BK 534-17-8 Cs2CO3
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28)	RCT	BV 870075-26-6
	RGT	W 7647-01-0 HCl
	PRO	BW 870075-27-7
	SOL	7732-18-5 Water
	NTE	regioselective

RX(29) RCT BW 870075-27-7

STAGE (1) RGT K 7553-56-2 I2, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE (2)

RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

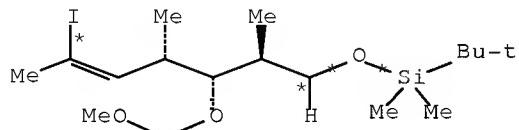
PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H2
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)₂

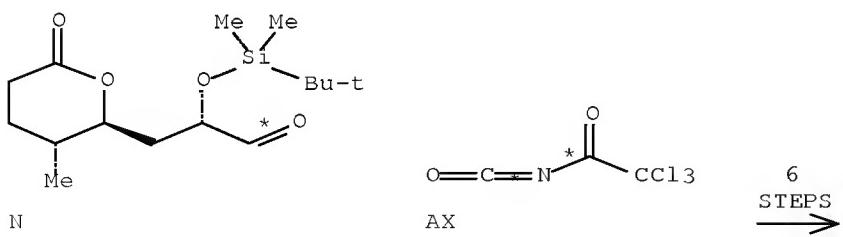
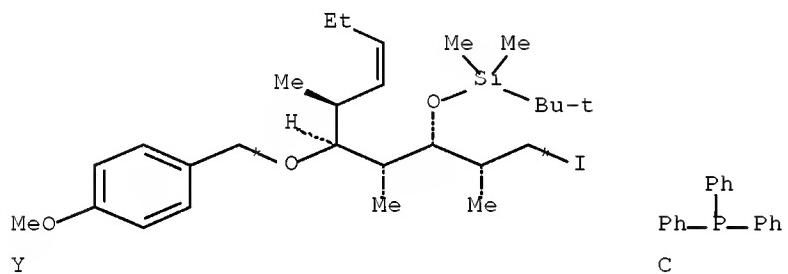
SOL 141-78-6 AcOEt
NTE Wittig coupling

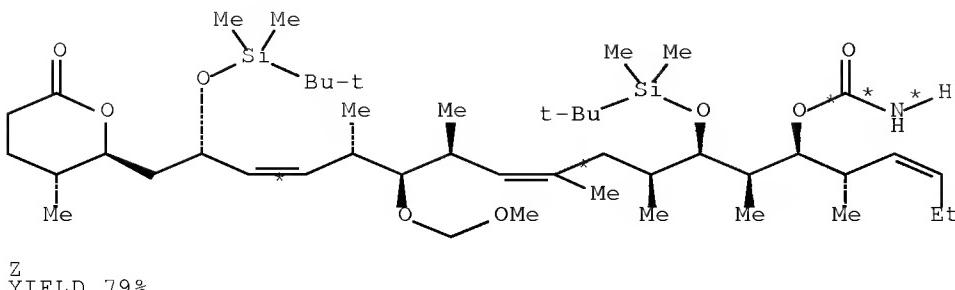
RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

RX(209) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31), RX(32)
RX(209) BI + Y + C + N + AX ==> Z

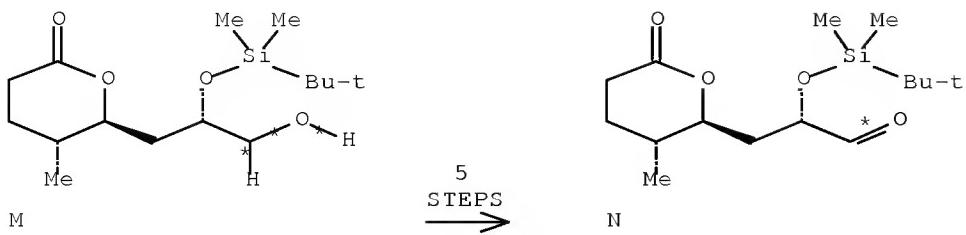
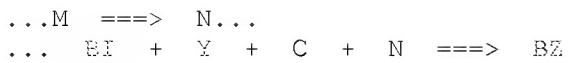


BI

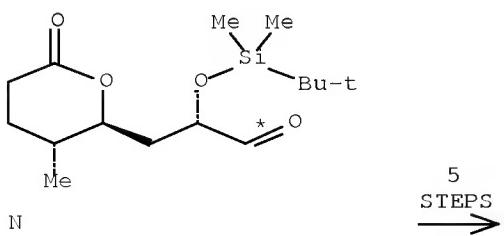
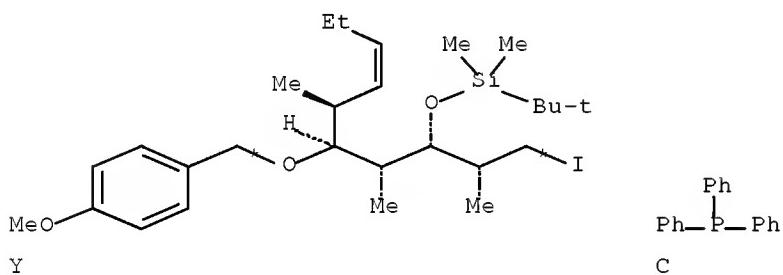
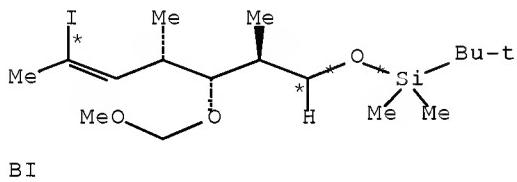


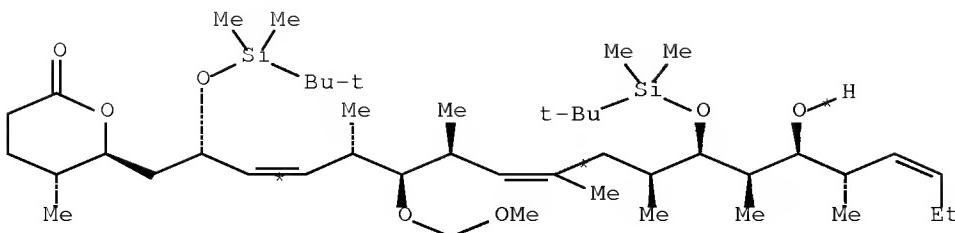


- RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling
- RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective
- RX(29) RCT BW 870075-27-7
- STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole
- STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C
- PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage
- RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt
 NTE Wittig coupling
- RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2
- RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation
- RX(217) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(30), RX(31)
 AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31)



START NEXT REACTION SEQUENCE





BZ
YIELD 93%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8

RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6

RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

PRO BX 870075-28-8

NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8

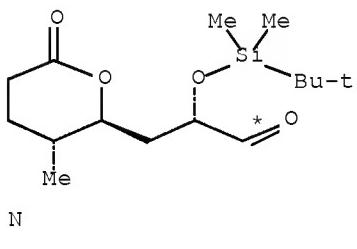
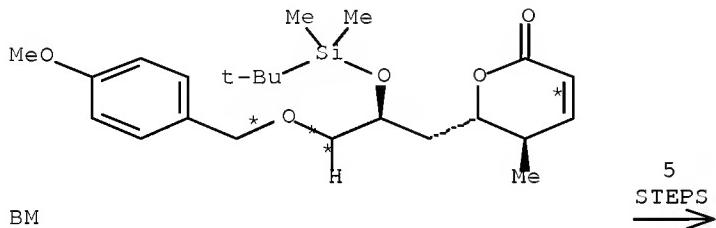
RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂

SOL 141-78-6 AcOEt
NTE Wittig coupling

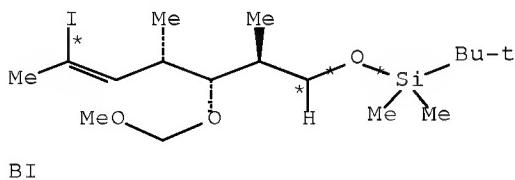
RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

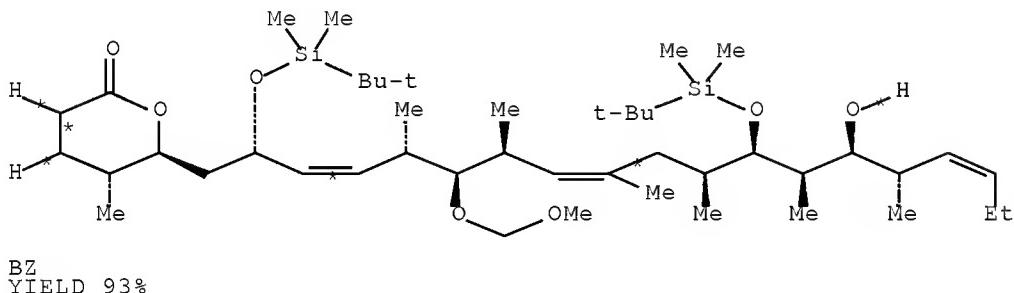
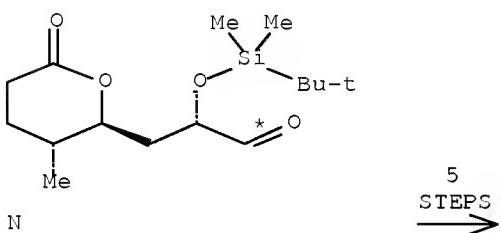
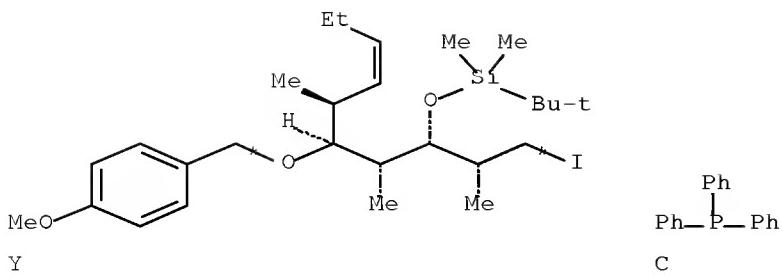
RX(218) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31)
AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31)

...BM ==> N...
... BI + Y + C + N ==> BZ



START NEXT REACTION SEQUENCE





BZ
YIELD 93%

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H2
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
 RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH2Cl2
 CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8
 RGT BK 534-17-8 Cs₂CO₃
 PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et₃N
 CON 100 deg C

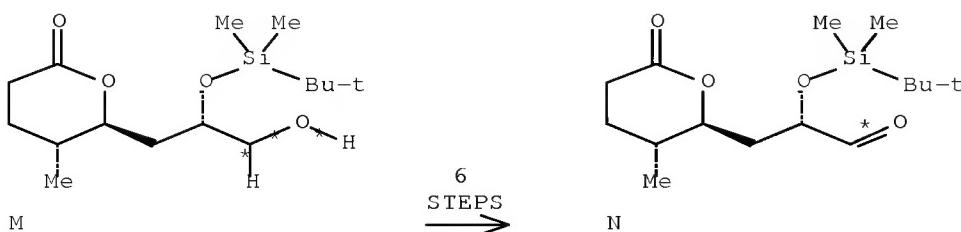
PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H₂
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt
 NTE Wittig coupling

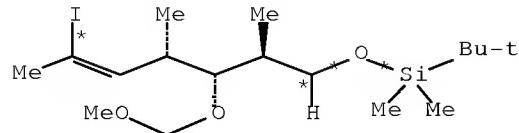
RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

RX(219) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(30), RX(31), RX(32)
 AND REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30), RX(31),
 RX(32)

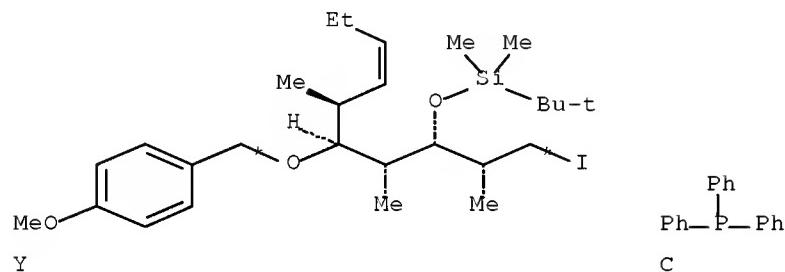
...M ==> N...
 ... BI + Y + C + N + AX ==> Z



START NEXT REACTION SEQUENCE

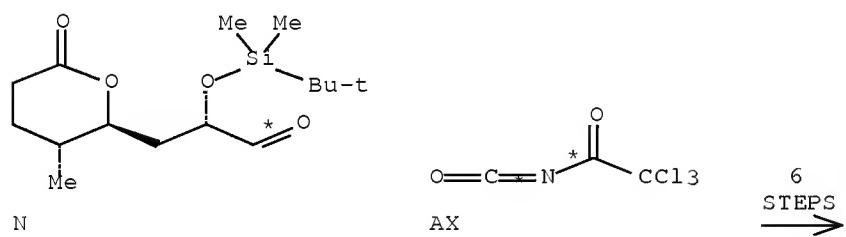


BI



Y

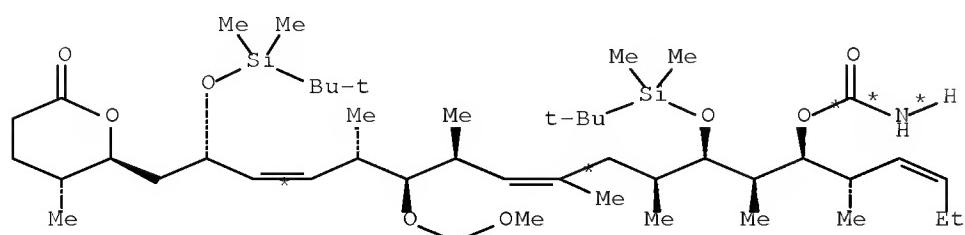
C



N

AX

6 STEPS



Z
YIELD 79%

RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(27) RCT BI 852049-56-0, Y 870075-02-8

RGT BK 534-17-8 Cs₂CO₃

PRO BV 870075-26-6

CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-

NTE Suzuki coupling

RX(28) RCT BV 870075-26-6

RGT W 7647-01-0 HCl

PRO BW 870075-27-7

SOL 7732-18-5 Water

NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)

RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et₃N

CON 100 deg C

PRO BX 870075-28-8

NTE stereoselective, Wittig salt formation in second stage

RX(30) RCT N 853055-22-8, BX 870075-28-8

RGT AU 1333-74-0 H₂

PRO BY 870075-29-9

CAT 12135-22-7 Pd(OH)₂

SOL 141-78-6 AcOEt

NTE Wittig coupling

RX(31) RCT BY 870075-29-9

RGT T 84-58-2 DDQ

PRO BZ 870075-30-2

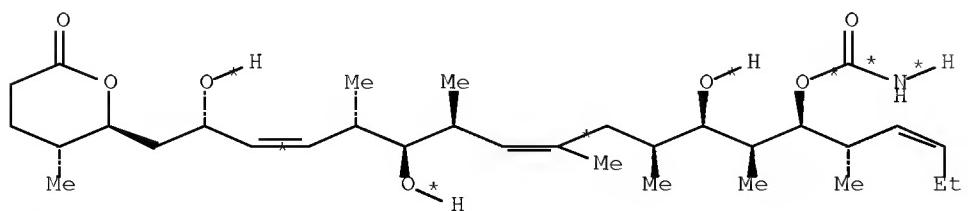
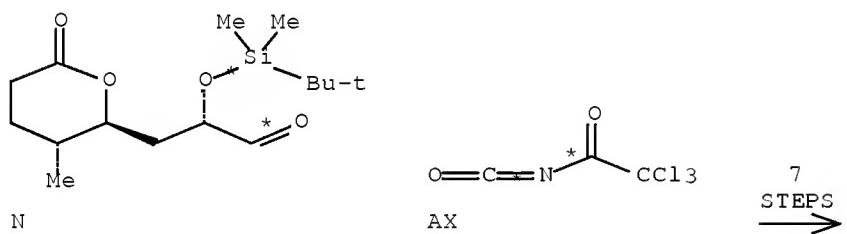
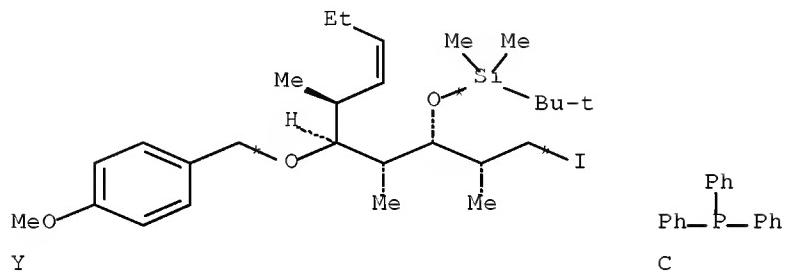
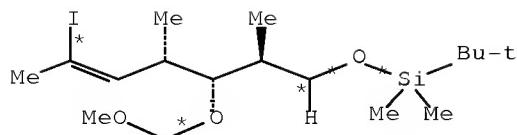
RX(32) RCT BZ 870075-30-2, AX 3019-71-4

PRO Z 870075-31-3

NTE literature preparation

RX(220) OF 268 COMPOSED OF RX(27), RX(28), RX(29), RX(30), RX(31), RX(32),
RX(7)

RX(220) BI + Y + C + N + AX ==> AA



AA
YIELD 70%

RX(27) RCT BI 852049-56-0, Y 870075-02-3
RG T BK 534-17-8 Cs₂CO₃

PRO BV 870075-26-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
 RGT W 7647-01-0 HCl
 PRO BW 870075-27-7
 SOL 7732-18-5 Water
 NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
 RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
 RCT C 603-35-0
 RGT L 121-44-8 Et3N
 CON 100 deg C

PRO BX 870075-28-8
 NTE stereoselective, Wittig salt formation in second stage

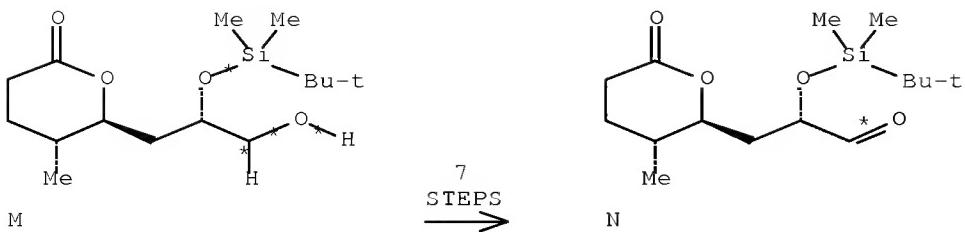
RX(30) RCT N 853055-22-8, BX 870075-28-8
 RGT AU 1333-74-0 H2
 PRO BY 870075-29-9
 CAT 12135-22-7 Pd(OH)2
 SOL 141-78-6 ACOEt
 NTE Wittig coupling

RX(31) RCT BY 870075-29-9
 RGT T 84-58-2 DDQ
 PRO BZ 870075-30-2

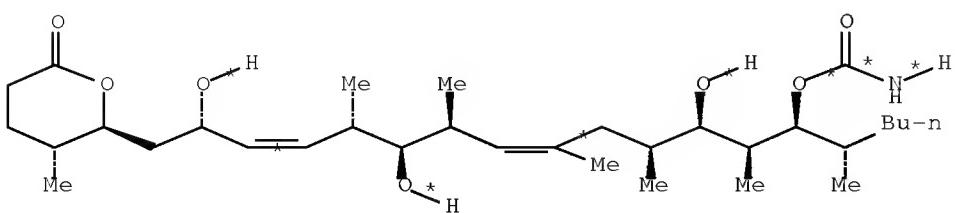
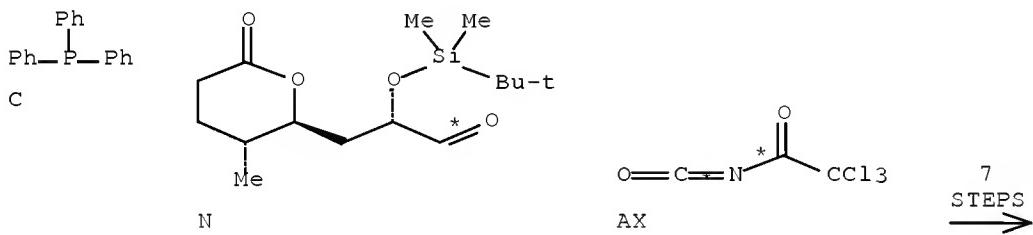
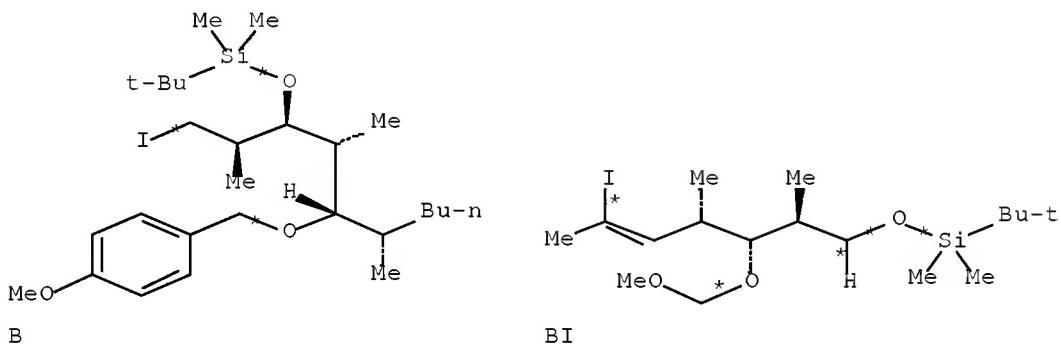
RX(32) RCT BZ 870075-30-2, AX 3019-71-4
 PRO Z 870075-31-3
 NTE literature preparation

RX(7) RCT Z 870075-31-3
 RGT W 7647-01-0 HCl
 PRO AA 870075-03-9
 SOL 7732-18-5 Water
 NTE yield over 8 steps = 17%

RX(236) OF 268 COMPOSED OF REACTION SEQUENCE RX(3), RX(23), RX(4), RX(24),
 RX(5)
 AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),
 RX(24), RX(5)
 ...M ==> N...
 ... B + BI + C + N + AX ==> V



START NEXT REACTION SEQUENCE



RX(3) RCT M 870075-20-0

STAGE(1)

RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)

RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0

RGT BK 534-17-8 Cs₂CO₃

PRO BJ 870075-18-6

CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-

NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6

RGT W 7647-01-0 HCl

PRO I 870075-19-7

SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et₃N

CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

PRO R 870075-21-1

NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1

RGT T 84-58-2 DDQ

PRO S 870075-00-6

NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4

PRO U 870075-22-2

NTE literature preparation

RX(5) RCT U 870075-22-2

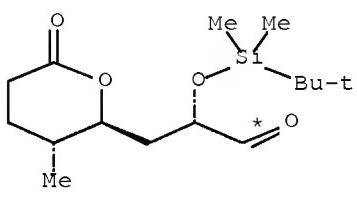
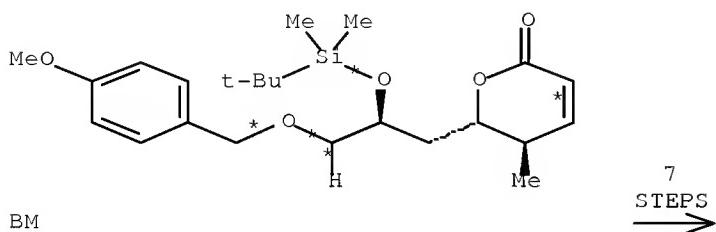
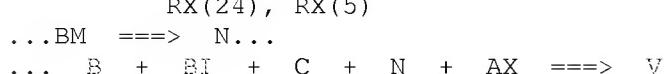
RGT W 7647-01-0 HCl

PRO V 870075-01-7

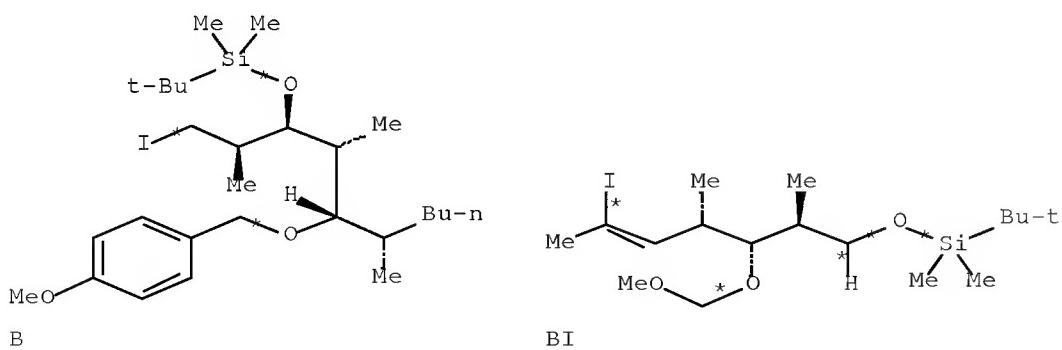
SOL 7732-18-5 Water

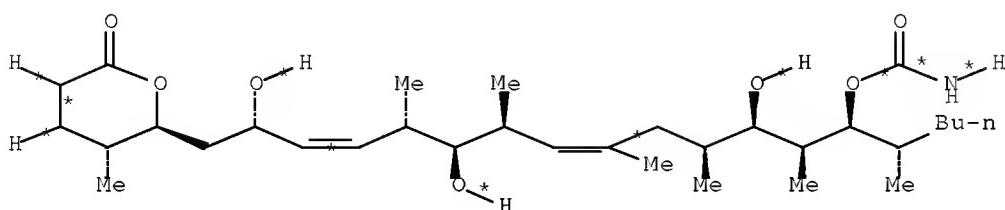
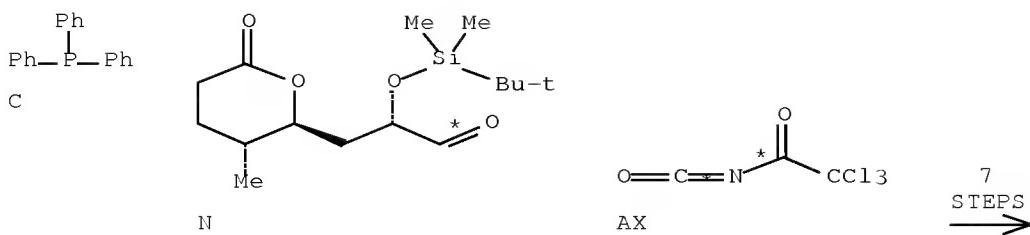
NTE yield over 2 steps = 54%

RX(237) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4),
RX(24), RX(5)
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),
RX(24), RX(5)



START NEXT REACTION SEQUENCE





V
YIELD 63%

RX(22) RCT BM 837383-29-6
 RGT AU 1333-74-0 H₂
 PRO M 870075-20-0
 CAT 12135-22-7 Pd(OH)₂
 SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE (1)
 RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
 SOL 75-09-2 CH₂Cl₂
 CON 2.5 hours, room temperature

STAGE (2)
 RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
 RGT BK 534-17-8 Cs₂CO₃
 PRO BJ 870075-18-6
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
 κP)ferrocene]dichloro-, (SP-4-2)-
 NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
 RGT W 7647-01-0 HCl
 PRO I 870075-19-7
 SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)

RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)

RCT C 603-35-0

RGT L 121-44-8 Et3N

CON 100 deg C

PRO J 870074-99-0

NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8

RGT AI 917-54-4 MeLi

PRO R 870075-21-1

NTE stereoselective, Wittig coupling

RX(4) RCT R 870075-21-1

RGT T 84-58-2 DDQ

PRO S 870075-00-6

NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4

PRO U 870075-22-2

NTE literature preparation

RX(5) RCT U 870075-22-2

RGT W 7647-01-0 HCl

PRO V 870075-01-7

SOL 7732-18-5 Water

NTE yield over 2 steps = 54%

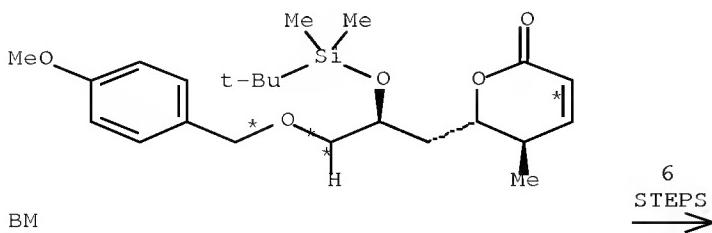
RX(238) OF 268 COMPOSED OF REACTION SEQUENCE RX(22), RX(3), RX(23), RX(4),
RX(24)

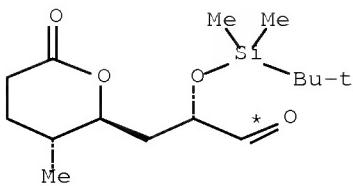
AND REACTION SEQUENCE RX(20), RX(21), RX(2), RX(23), RX(4),

RX(24)

...BM ==> N...

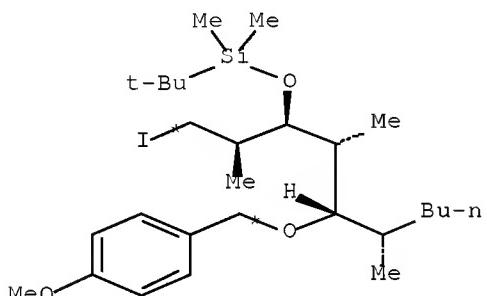
... B + BI + C + N + AX ==> U



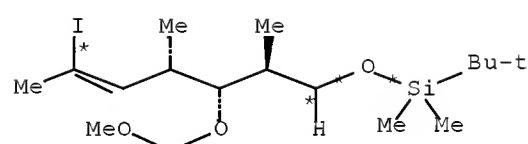


N

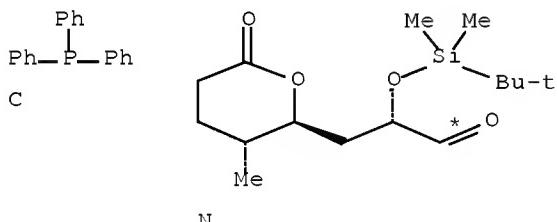
START NEXT REACTION SEQUENCE



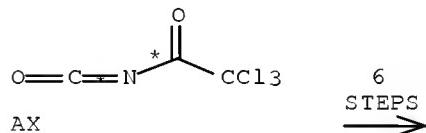
B



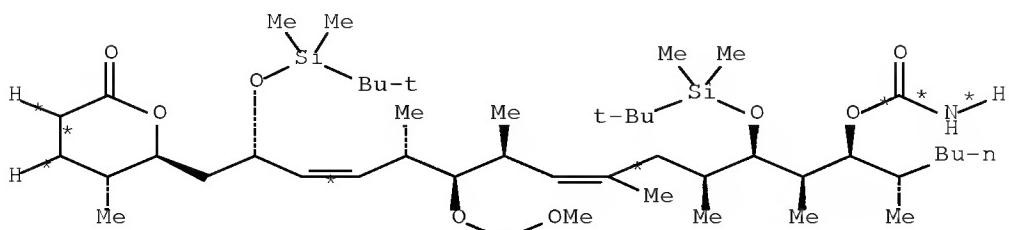
BI



C



6 STEPS →



^U
YIELD 85%

RX(22) RCT BM 837383-29-6
RGT AU 1333-74-0 H2
PRO M 870075-20-0
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(20) RCT B 870074-98-9, BI 852049-56-0
RGT BK 534-17-8 Cs2CO3
PRO BJ 870075-18-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(21) RCT BJ 870075-18-6
RGT W 7647-01-0 HCl
PRO I 870075-19-7
SOL 7732-18-5 Water

RX(2) RCT I 870075-19-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO J 870074-99-0
NTE Wittig salt formation in second stage, yield over 4 steps = 65%

RX(23) RCT J 870074-99-0, N 853055-22-8
RGT AI 917-54-4 MeLi
PRO R 870075-21-1
NTE stereoselective, Wittig coupling

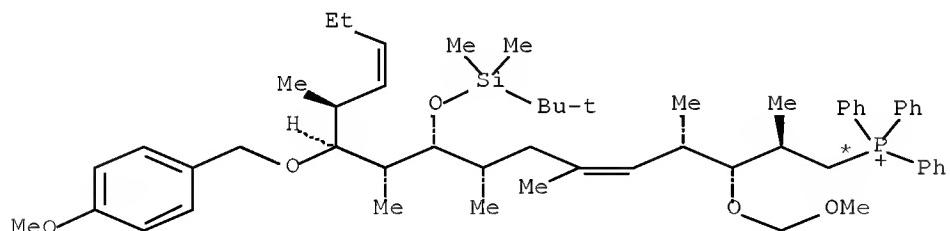
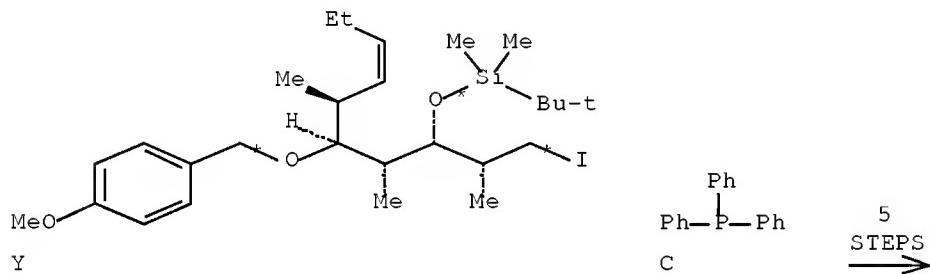
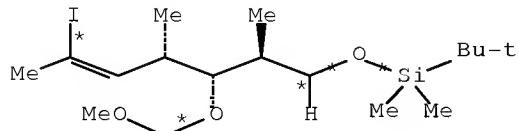
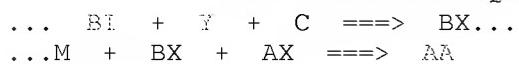
RX(4) RCT R 870075-21-1
RGT T 84-58-2 DDQ
PRO S 870075-00-6
NTE yield over 2 steps = 36%

RX(24) RCT S 870075-00-6, AX 3019-71-4
PRO U 870075-22-2

NTE literature preparation

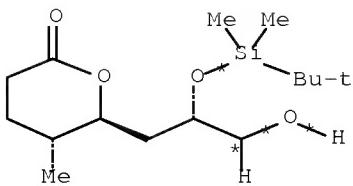
RX(248) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
RX(31), RX(32), RX(7)

AND REACTION SEQUENCE RX(3), RX(30), RX(31), RX(32), RX(7)

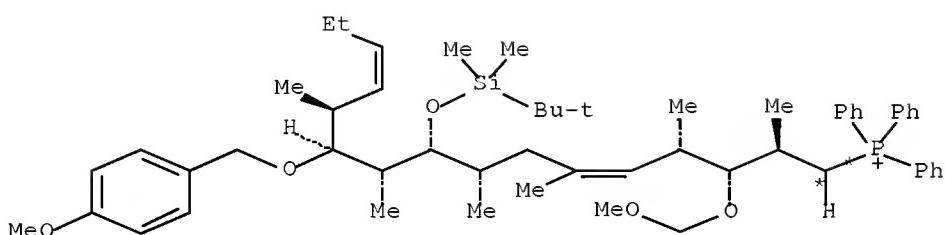


BX

START NEXT REACTION SEQUENCE

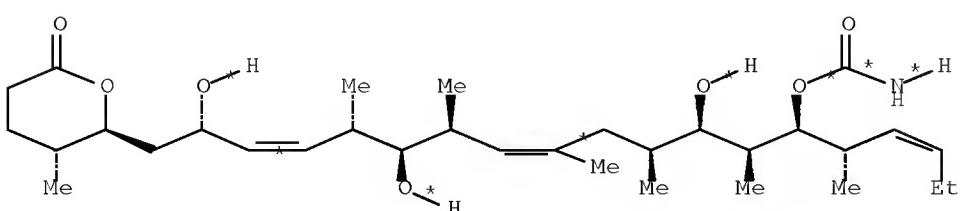
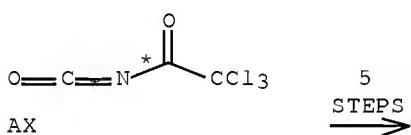


M



● I⁻

BX



AA
YIELD 70%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RG T BK 534-17-8 Cs₂CO₃

PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2Cl2
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H2
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt
NTE Wittig coupling

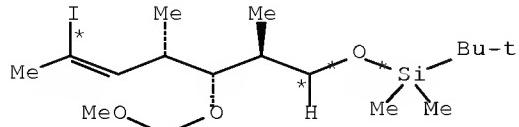
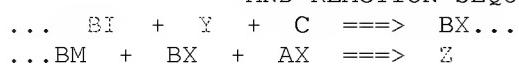
RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
PRO Z 870075-31-3
NTE literature preparation

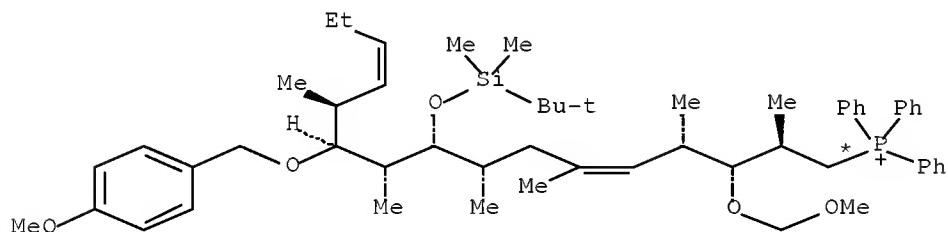
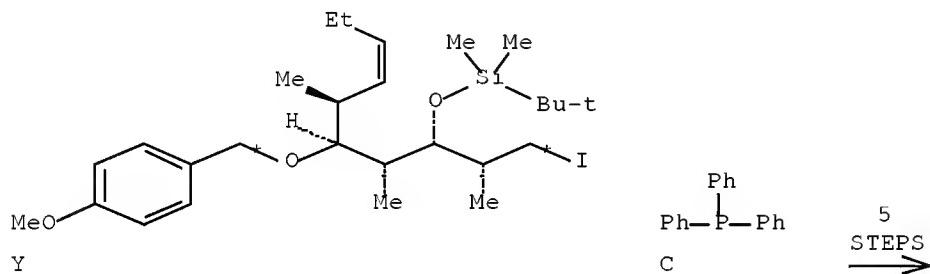
RX(7) RCT Z 870075-31-3
RGT W 7647-01-0 HCl
PRO AA 870075-03-9
SOL 7732-18-5 Water
NTE yield over 8 steps = 17%

RX(254) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
RX(31), RX(32)

AND REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31), RX(32)



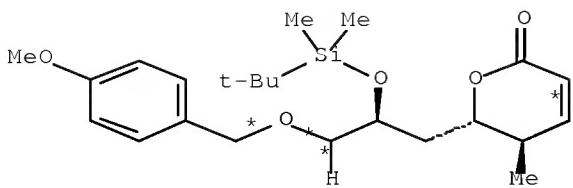
BI



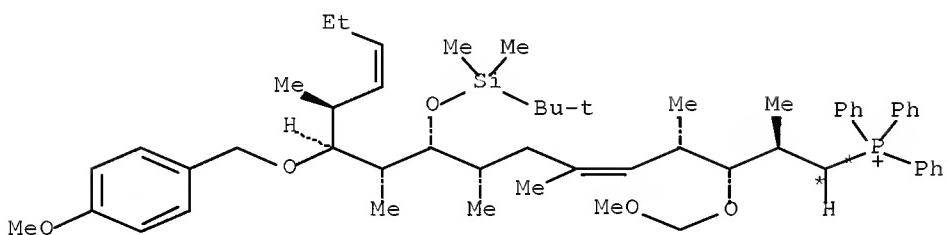
● I-

BX

START NEXT REACTION SEQUENCE

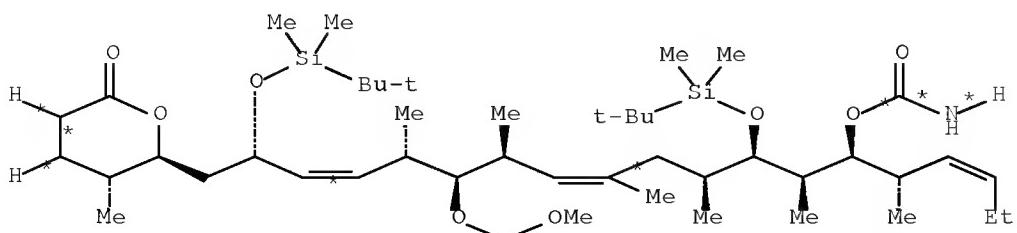
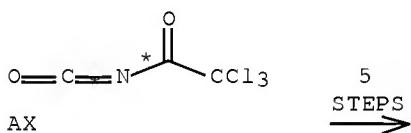


BM



● I⁻

BX



Z
YIELD 79%

RX(27) RCT BI 852049-56-0, Y 870075-02-8

RGT BK 534-17-8 Cs₂CO₃
PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
RGT K 7553-56-2 I₂, C 603-35-0 PPh₃, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et₃N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
RGT AU 1333-74-0 H₂
PRO M 870075-20-0
CAT 12135-22-7 Pd(OH)₂
SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO₃, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH₂Cl₂
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na₂S₂O₃, E 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

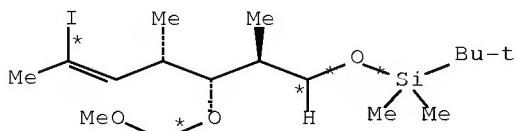
PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H₂
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)₂
SOL 141-78-6 AcOEt
NTE Wittig coupling

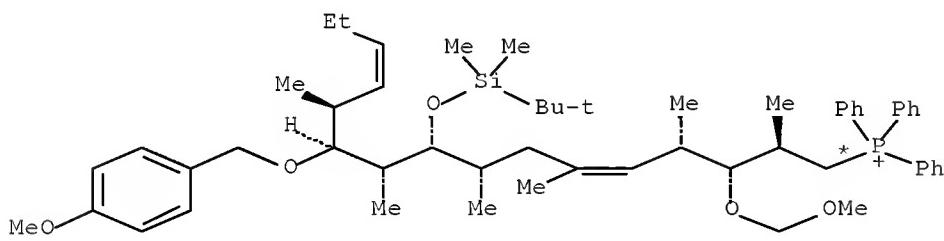
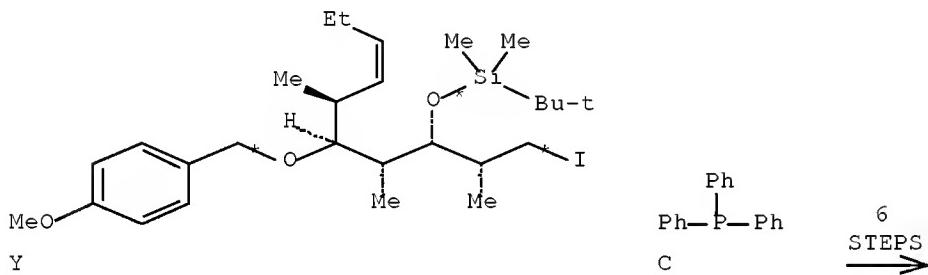
RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
PRO Z 870075-31-3
NTE literature preparation

RX(258) OF 268 COMPOSED OF REACTION SEQUENCE RX(27), RX(28), RX(29), RX(30),
 RX(31), RX(32), RX(7)
 AND REACTION SEQUENCE RX(22), RX(3), RX(30), RX(31), RX(32),
 RX(7)
 ... BI + Y + C ==> BX...
 ... BM + BX + AX ==> AA

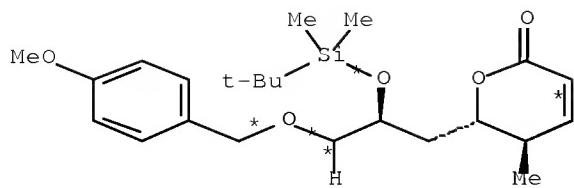


BI

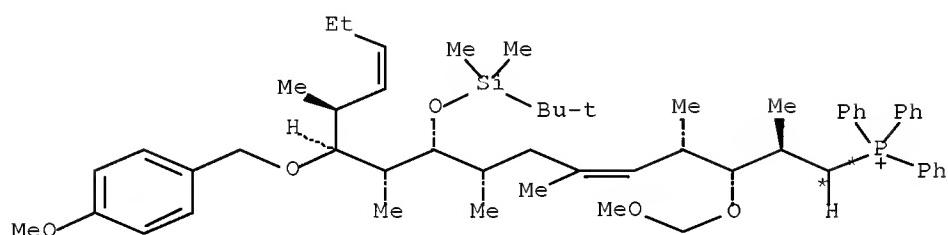


BX

START NEXT REACTION SEQUENCE

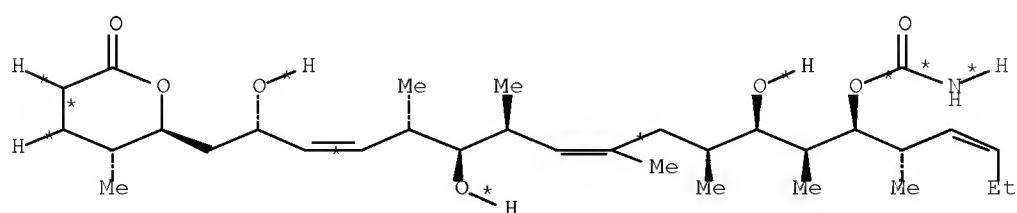
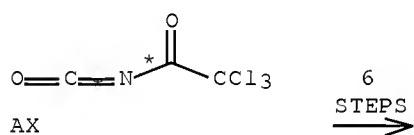


BM



● I⁻

BX



AA
YIELD 70%

RX(27) RCT BI 852049-56-0, Y 870075-02-8
RG T BK 534-17-8 Cs₂CO₃

PRO BV 870075-26-6
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-
κP)ferrocene]dichloro-, (SP-4-2)-
NTE Suzuki coupling

RX(28) RCT BV 870075-26-6
RGT W 7647-01-0 HCl
PRO BW 870075-27-7
SOL 7732-18-5 Water
NTE regioselective

RX(29) RCT BW 870075-27-7

STAGE(1)
RGT K 7553-56-2 I2, C 603-35-0 PPh3, D 288-32-4 1H-Imidazole

STAGE(2)
RCT C 603-35-0
RGT L 121-44-8 Et3N
CON 100 deg C

PRO BX 870075-28-8
NTE stereoselective, Wittig salt formation in second stage

RX(22) RCT BM 837383-29-6
RGT AU 1333-74-0 H2
PRO M 870075-20-0
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt

RX(3) RCT M 870075-20-0

STAGE(1)
RGT E 144-55-8 NaHCO3, O 87413-09-0 Martin's reagent
SOL 75-09-2 CH2C12
CON 2.5 hours, room temperature

STAGE(2)
RGT P 7772-98-7 Na2S2O3, E 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO N 853055-22-8

RX(30) RCT N 853055-22-8, BX 870075-28-8
RGT AU 1333-74-0 H2
PRO BY 870075-29-9
CAT 12135-22-7 Pd(OH)2
SOL 141-78-6 AcOEt
NTE Wittig coupling

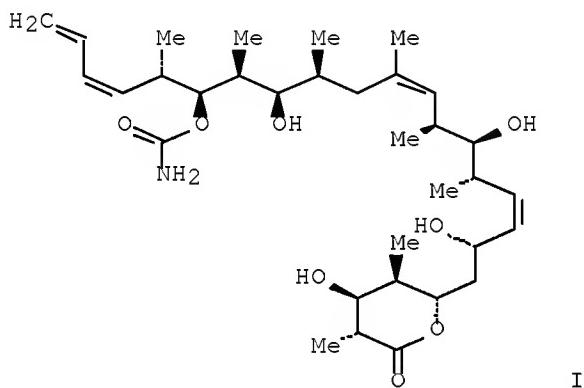
RX(31) RCT BY 870075-29-9
RGT T 84-58-2 DDQ
PRO BZ 870075-30-2

RX(32) RCT BZ 870075-30-2, AX 3019-71-4
PRO Z 870075-31-3
NTE literature preparation

RX(7) RCT Z 870075-31-3

RGT W 7647-01-0 HCl
PRO AA 870075-03-9
SOL 7732-18-5 Water
NTE yield over 8 steps = 17%

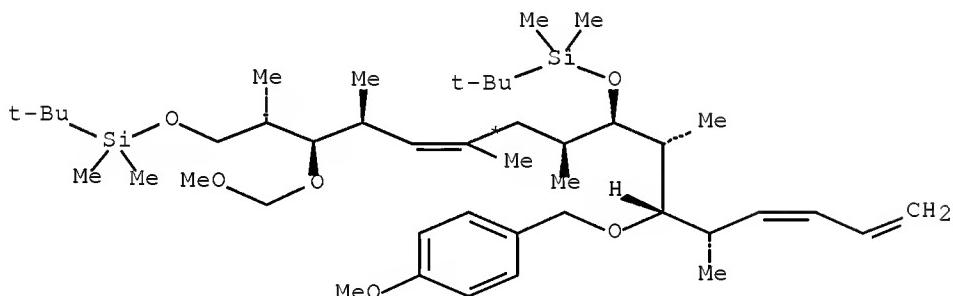
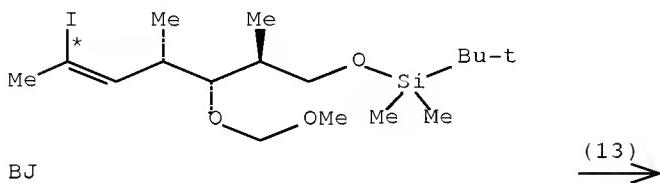
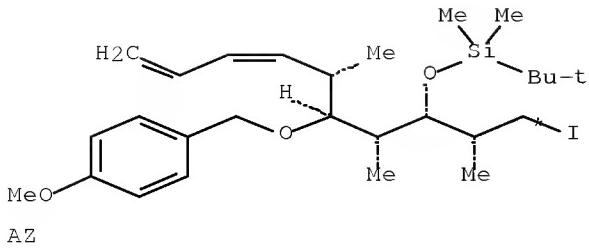
L3 ANSWER 5 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:481865 CASREACT [Full-text](#)
TITLE: Total Synthesis of (+)-Discodermolide: A Highly
Convergent Fourth-Generation Approach
AUTHOR(S): Smith, Amos B., III; Freeze, B. Scott; Xian, Ming;
Hirose, Tomoyasu
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania,
Philadelphia, PA, 19104, USA
SOURCE: Organic Letters (2005), 7(9), 1825-1828
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A highly convergent, fourth-generation total synthesis of (+)-discodermolide (I), with a longest linear sequence of 17 steps and an overall yield of 9.0%, has been achieved. Highlighting the strategy is the efficient construction and sequential, bidirectional union of a linchpin comprising the C(9)-C(14) Wittig salt-vinyl iodide (-)-18. Importantly, Wittig salt generation proceeded in excellent yield under ambient pressure.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(13) OF 178 ...AZ + EJ ==> BL



BL
YIELD 79%

RX(13) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyihydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C \rightarrow room temperature
SUBSTAGE(3) 1 hour, room temperature

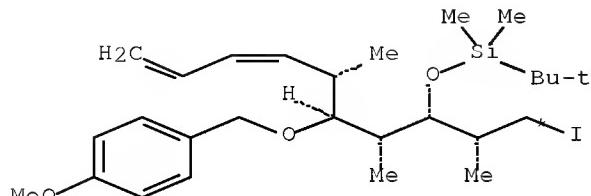
STAGE(2)

RCT BJ 852049-56-0
RGT BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,

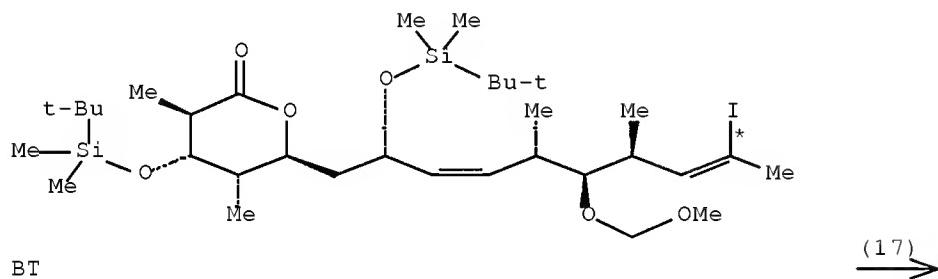
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO BL 633293-91-1
 NTE in the dark

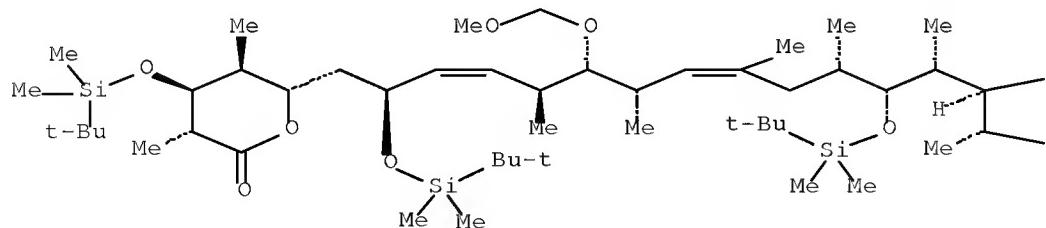
RX(17) OF 178 ...AZ + BT ==> EV

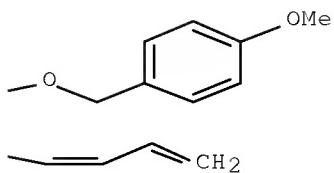


AZ



PAGE 1-A





BV
YIELD 40%

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldihydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

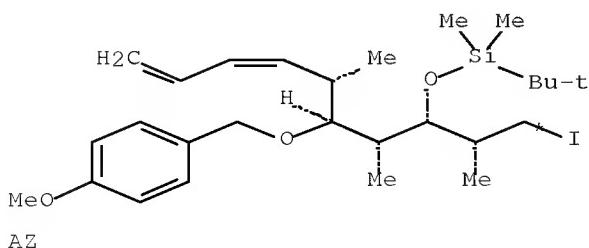
STAGE(2)

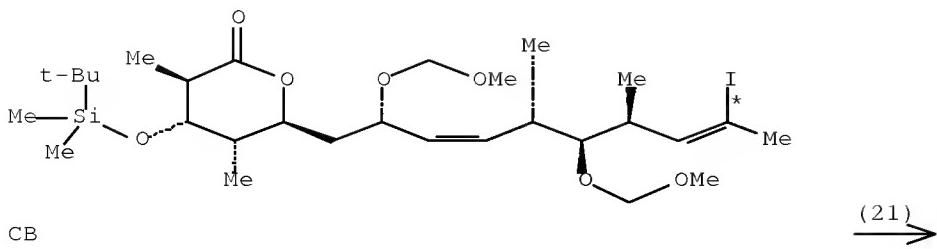
RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

PRO BV 633293-75-1

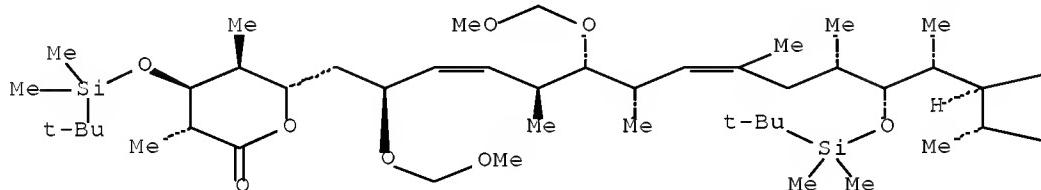
NTE in the dark

RX(21) OF 178 ...AZ + CB ==> CC...

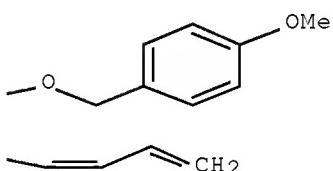




PAGE 1-A



PAGE 1-B



CC
YIELD 60%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldihydroxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C → room temperature
SUBSTAGE(3) 1 hour, room temperature

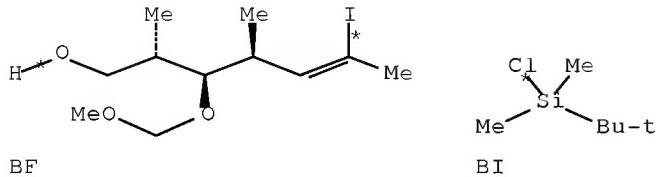
STAGE(2)

RCT CB 852049-53-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,

(SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

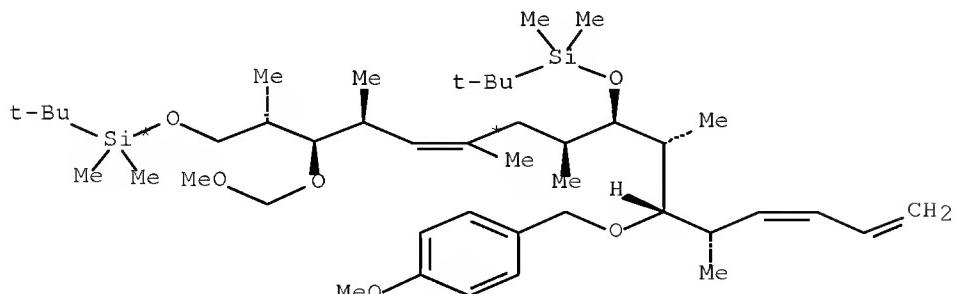
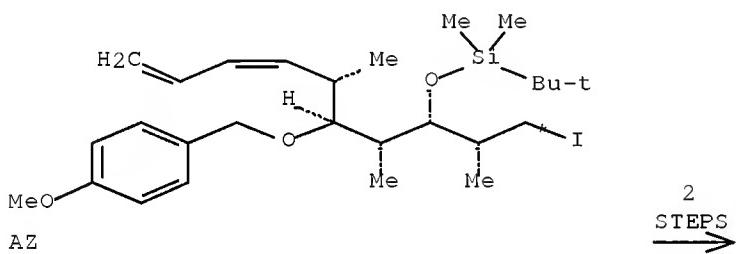
PRO CC 852049-59-3

RX(39) OF 178 COMPOSED OF RX(12), RX(13)
 RX(39) BF + BI + AZ ==> BL



BF

BI



BL
 YIELD 79%

RX(12) RCT BF 850211-70-0, BI 18162-48-6

STAGE (1)
 RGT BC 288-32-4 1H-Imidazole

SOL 75-09-2 CH₂Cl₂
CON 15 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BJ 852049-56-0

RX(13) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

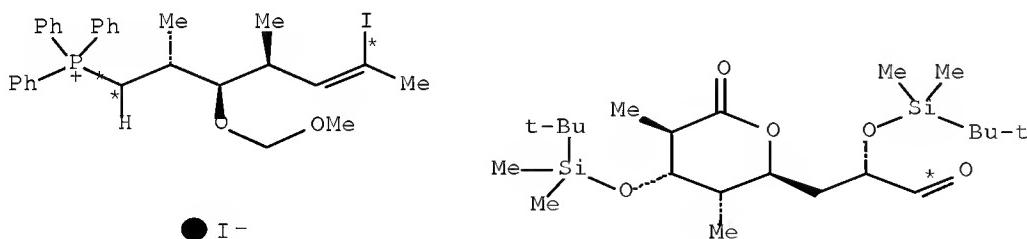
STAGE(2)

RCT BJ 852049-56-0
RGT BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO BL 633293-91-1

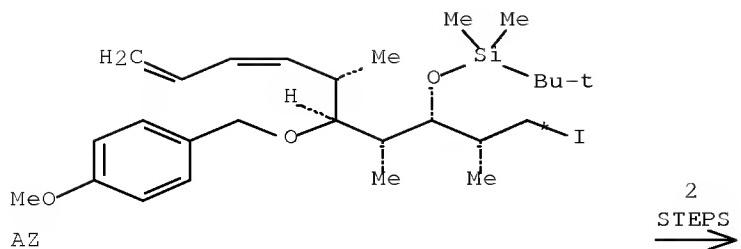
NTE in the dark

RX(43) OF 178 COMPOSED OF RX(16), RX(17)
RX(43) BR + BS + AZ ==> BV

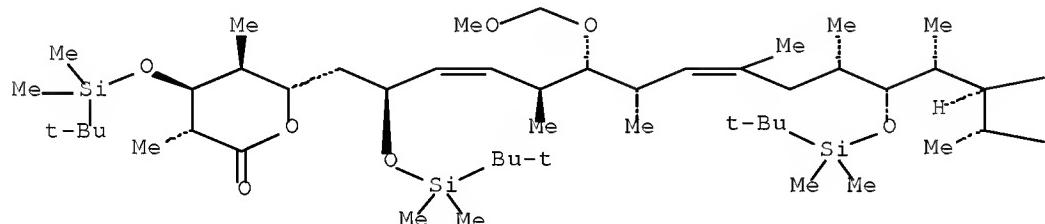


BR

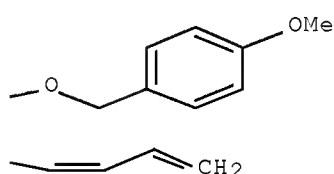
BS



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^{BV}
YIELD 40%

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

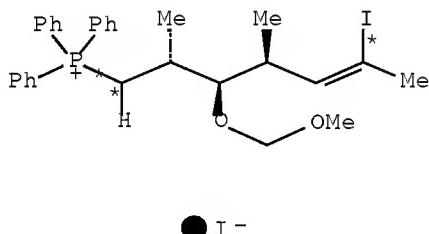
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldihydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

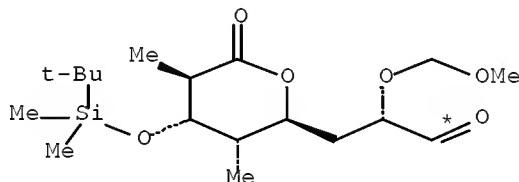
RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

PRO BV 633293-75-1
NTE in the dark

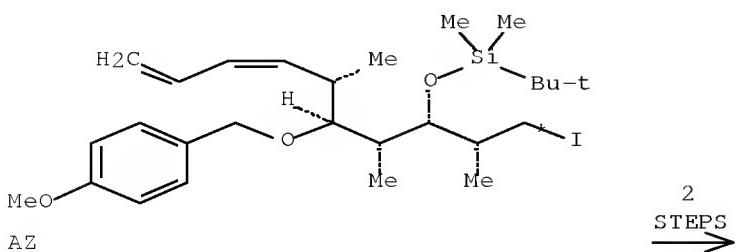
RX(46) OF 178 COMPOSED OF RX(20), RX(21)
RX(46) BF + CA + AZ ==> CC



BR



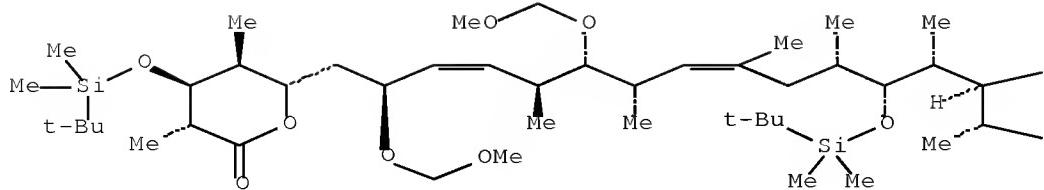
CA



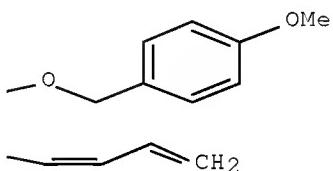
AZ

2 STEPS
 $\xrightarrow{ }$

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CC
YIELD 60%

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature

SUBSTAGE (3) 1 hour, room temperature

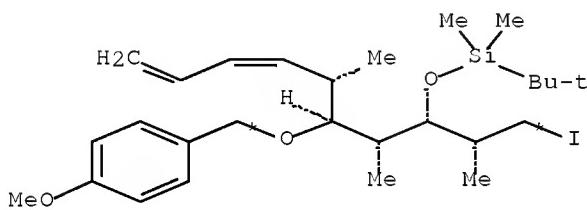
STAGE (2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

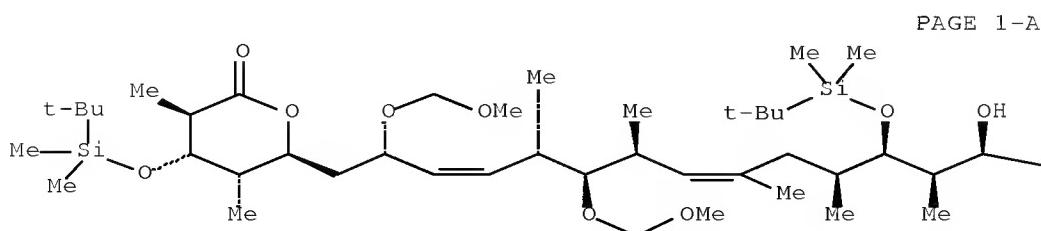
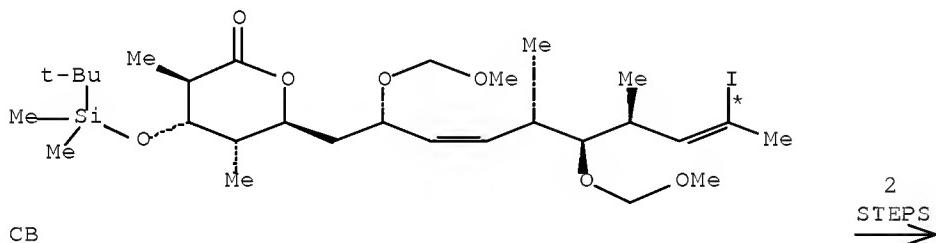
PRO CC 852049-59-3

RX(47) OF 178 COMPOSED OF RX(21), RX(22)

RX(47) AZ + CB ==> CD



AZ





^{CD}
YIELD 91%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

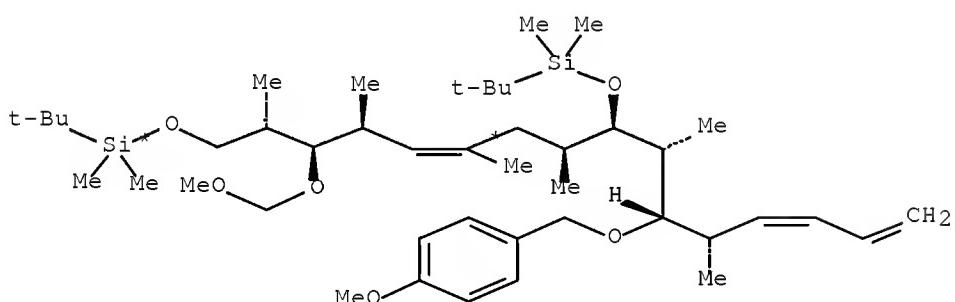
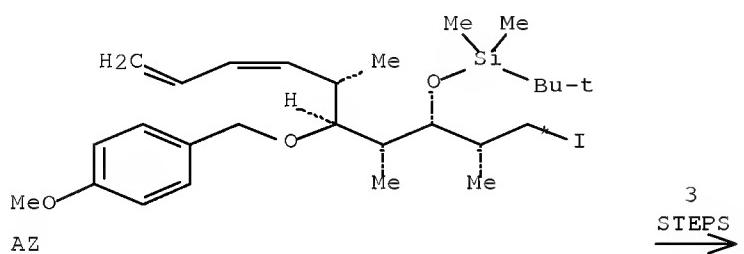
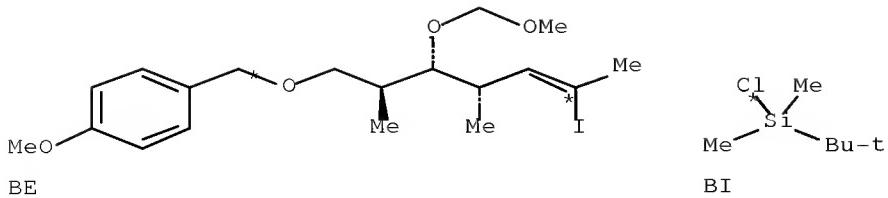
RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(73) OF 178 COMPOSED OF RX(11), RX(12), RX(13)
 RX(73) BE + BI + AZ ==> BL



BL
YIELD 79%

RX(11) RCT BE 633294-02-7

STAGE (1)

RGT BG 84-58-2 DDO
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 2 hours, 0 deg C

STAGE (2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(12) RCT BF 850211-70-0, BI 18162-48-6

STAGE(1)

RGT BC 288-32-4 1H-Imidazole
 SOL 75-09-2 CH₂Cl₂
 CON 15 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
 SOL 7732-18-5 Water
 CON room temperature

PRO BJ 852049-56-0

RX(13) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

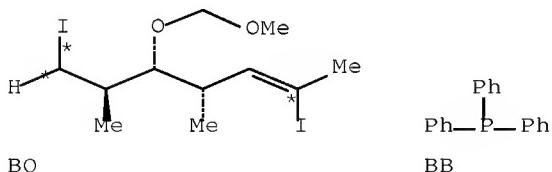
RCT BJ 852049-56-0
 RGT BN 534-17-8 Cs₂CO₃
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

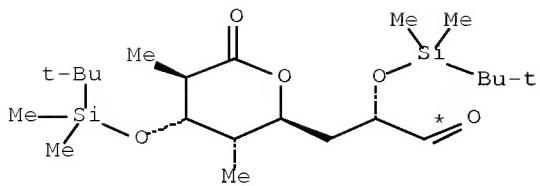
PRO BL 633293-91-1

NTE in the dark

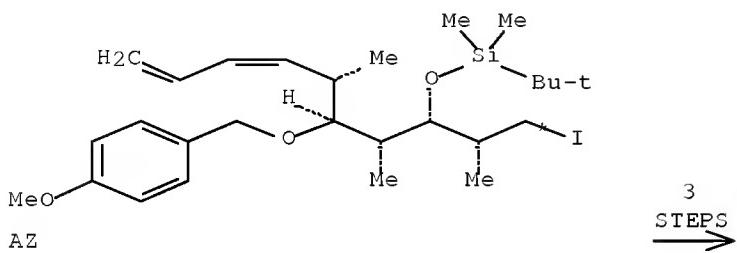
RX(79) OF 178 COMPOSED OF RX(15), RX(16), RX(17)

RX(79) BQ + BB + BS + AZ ==> BV



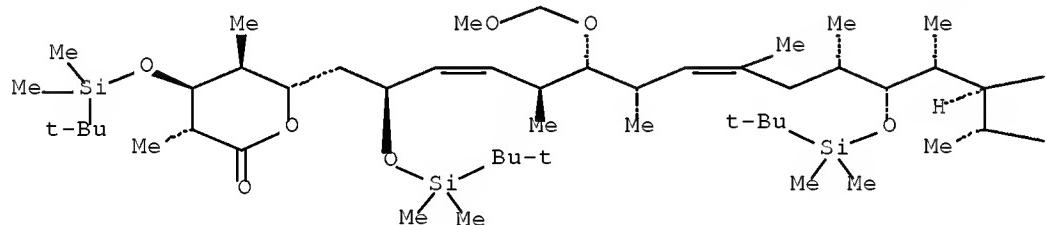


BS

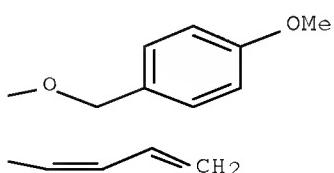


STEPS

PAGE 1-A



PAGE 1-B



BV
YIELD 40%

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2

CON SUBSTAGE(1) room temperature -> 95 deg C

SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

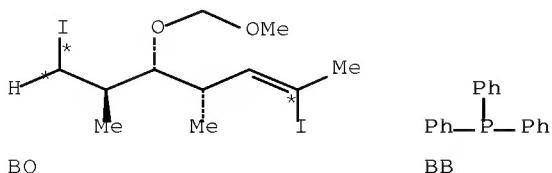
RCT BT 850211-74-4
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water
CON 20 hours, room temperature

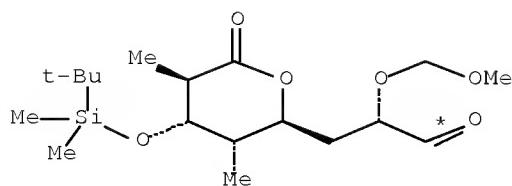
PRO BV 633293-75-1

NTE in the dark

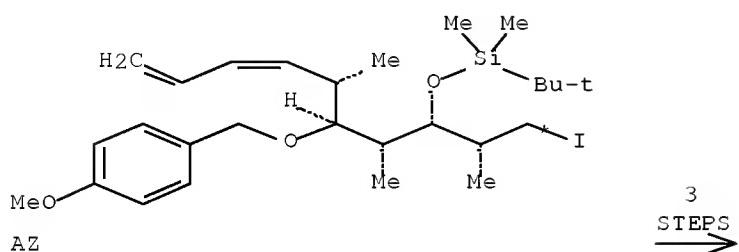
RX(80) OF 178 COMPOSED OF RX(15), RX(20), RX(21)

RX(80) BQ + BB + CA + AZ ==> CC

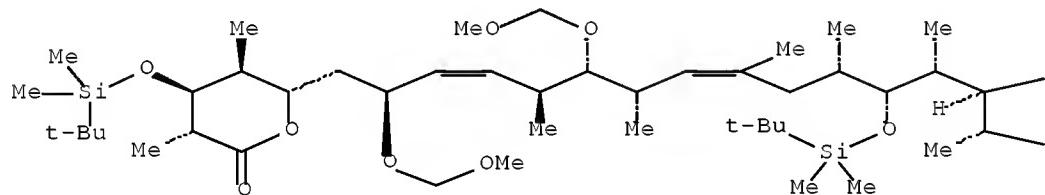




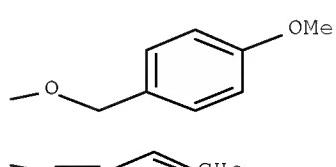
CA



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CC
YIELD 60%

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

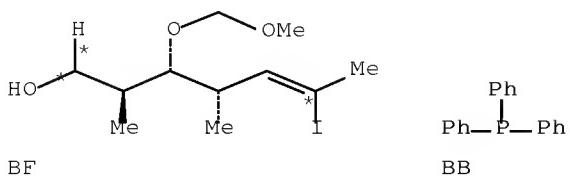
RX(21) RCT AZ 850211-69-7

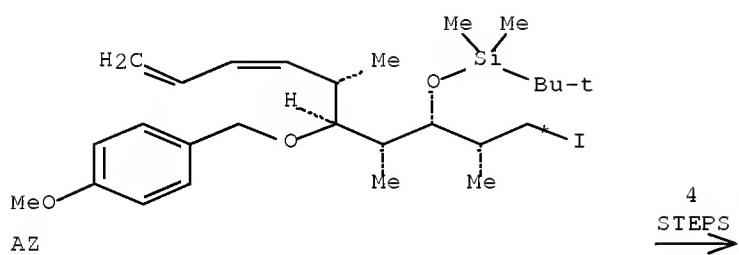
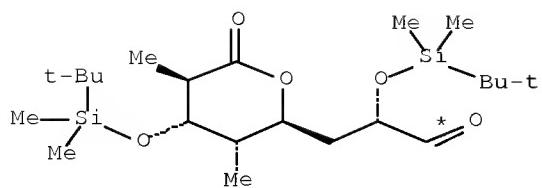
STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldihydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

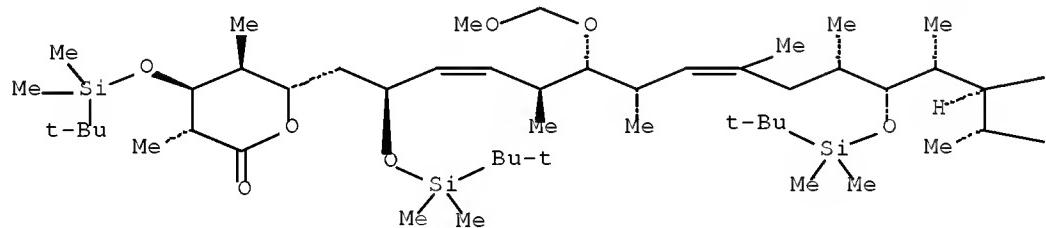
PRO CC 852049-59-3

RX(81) OF 178 COMPOSED OF RX(14), RX(15), RX(16), RX(17)
RX(81) BF + BB + BS + AZ ==> BV

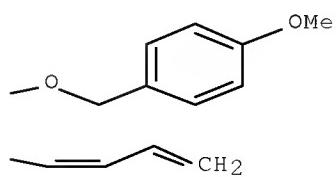




PAGE 1-A



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BV
YIELD 40%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT BS 252342-51-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO BT 850211-74-4

RX(17) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

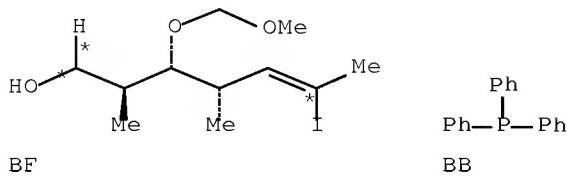
STAGE(2)

RCT BT 850211-74-4
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water

CON 20 hours, room temperature

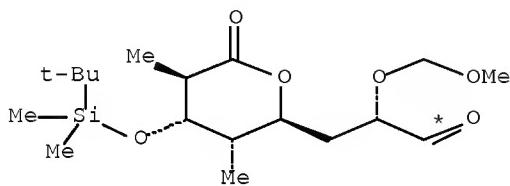
PRO BV 633293-75-1
NTE in the dark

RX(82) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21)
RX(82) BF + BB + CA + AZ ==> CC

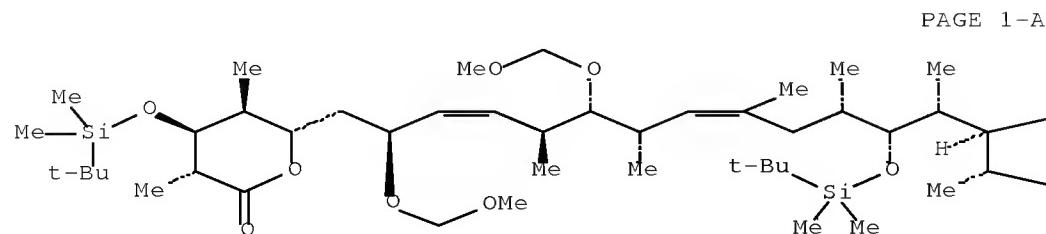
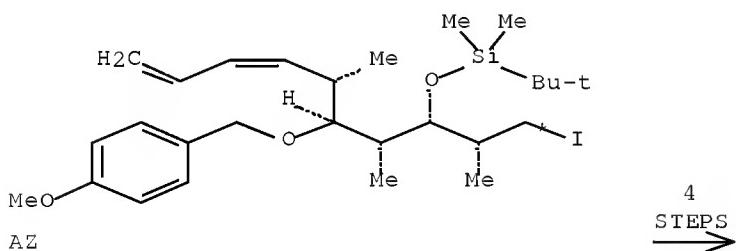


BF

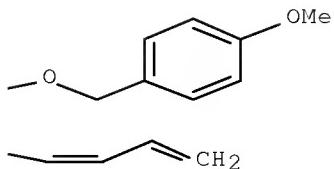
BB



CA



PAGE 1-A



^{CC}
YIELD 60%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et2O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane

CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C → room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-

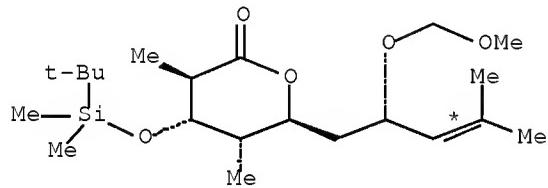
SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

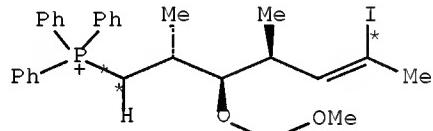
PRO CC 852049-59-3

RX(84) OF 178 COMPOSED OF RX(19), RX(20), RX(21)

RX(84) BZ + BR + AZ ==> CC

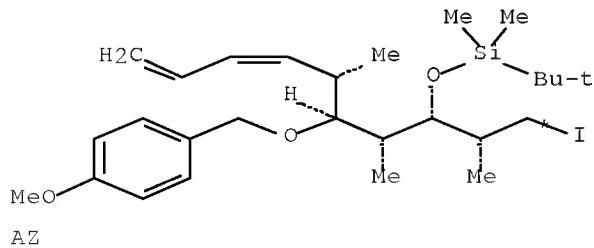


BZ



● I-

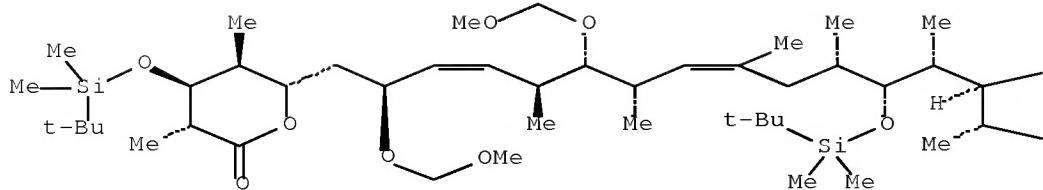
BR



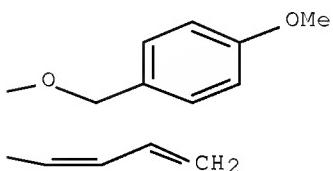
AZ

3
 STEPS

PAGE 1-A



PAGE 1-B



CC
YIELD 60%

RX(19) RCT BZ 852049-62-8

STAGE (1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂
CON -78 deg C

STAGE (2)

RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE (1)

RGT BU 1070-89-9 (Me_3Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE (2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE (3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

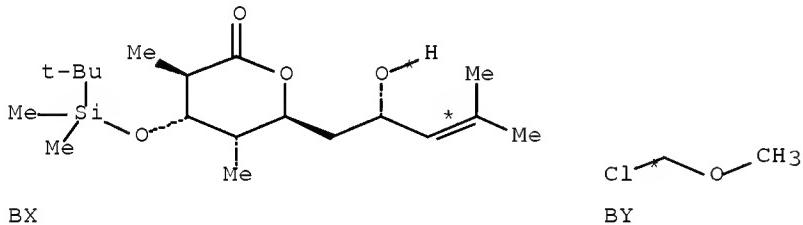
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

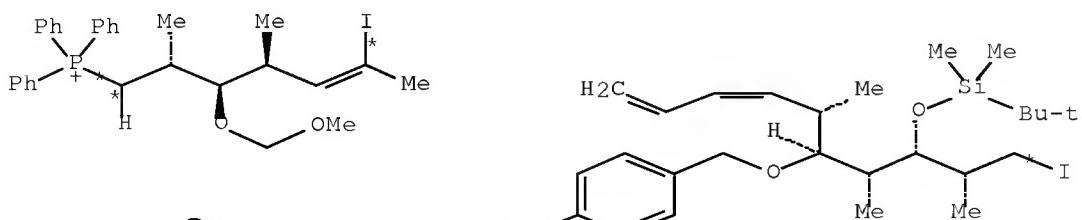
PRO CC 852049-59-3

RX(85) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21)
RX(85) BX + BY + BR + AZ ==> CC



BX

BY

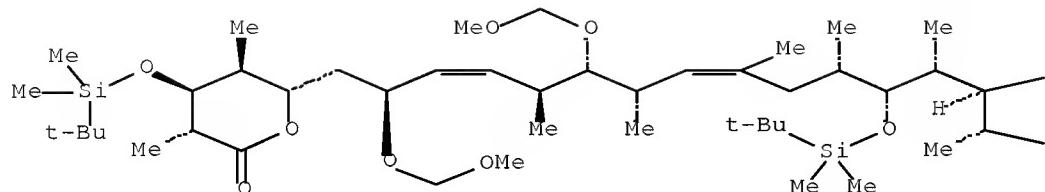


BR

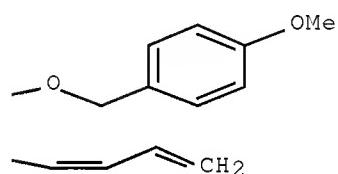
AZ

4
STEPS
→

PAGE 1-A



PAGE 1-B



CC
YIELD 60%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE (1)

RGT H 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH₂C₁₂
CON 12 hours, room temperature

STAGE (2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE (1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂
CON -78 deg C

STAGE (2)

RGT BB 603-35-0 PPh₃

CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na

SOL 109-99-9 THF

CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1

SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C

SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C

SUBSTAGE(2) -78 deg C -> room temperature

SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

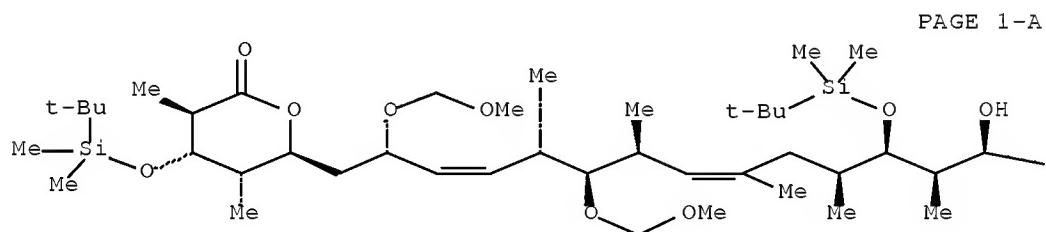
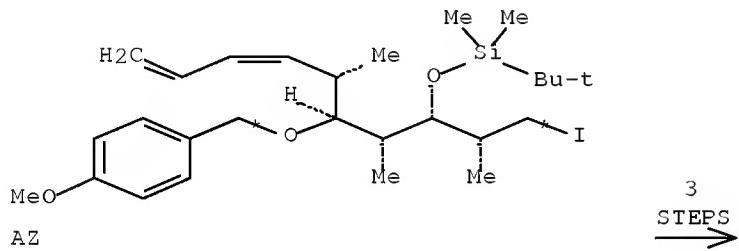
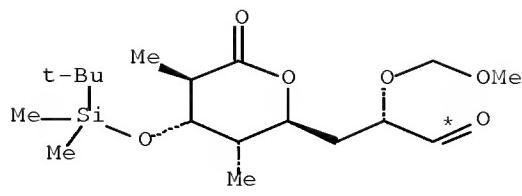
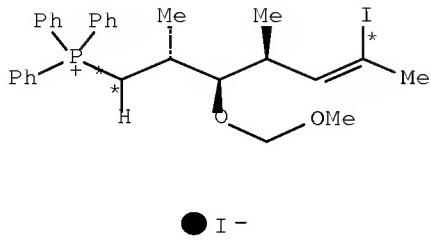
SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

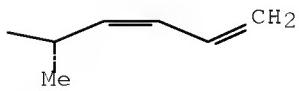
PRO CC 852049-59-3

RX(86) OF 178 COMPOSED OF RX(20), RX(21), RX(22)

RX(86) BP + CA + AZ ==> CD



PAGE 1-B



^{CD}
YIELD 91%

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me₃Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

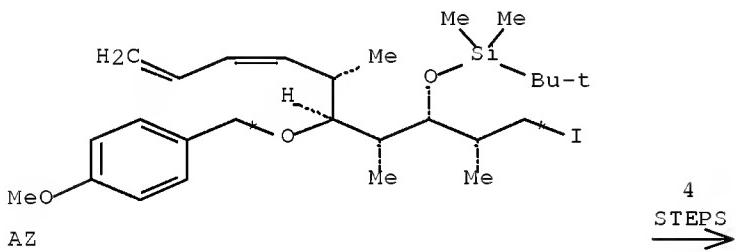
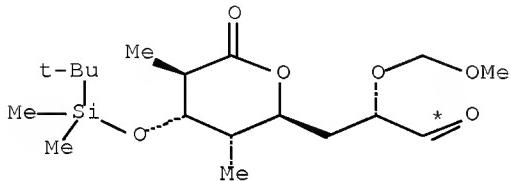
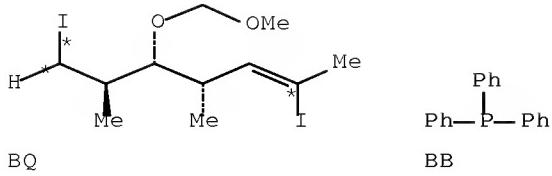
RX(22) RCT CC 852049-59-3

STAGE(1)
 RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

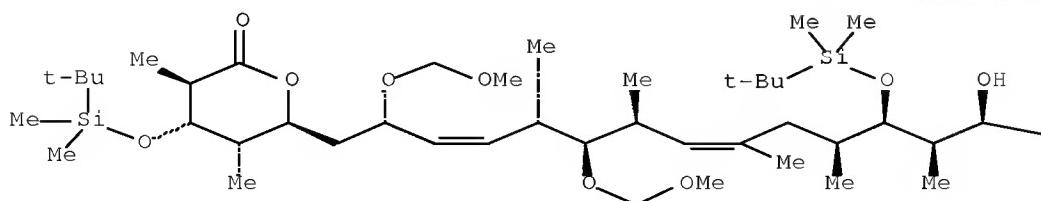
STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(87) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22)
 RX(87) BQ + BB + CA + AZ ==> CD



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^{CD}
YIELD 91%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

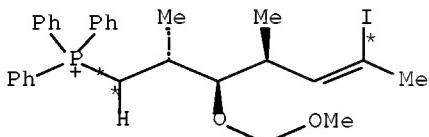
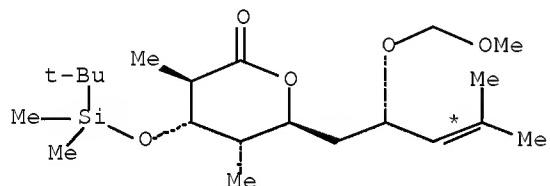
RG^T BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C → room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RG^T BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

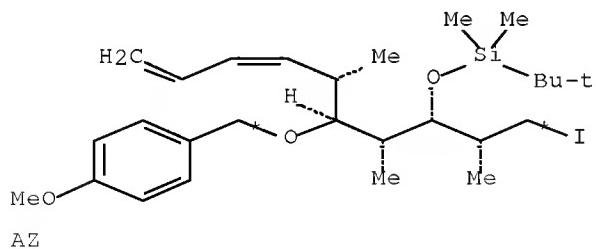
RX(88) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22)
RX(88) BZ + BR + AZ ==> CD



BZ

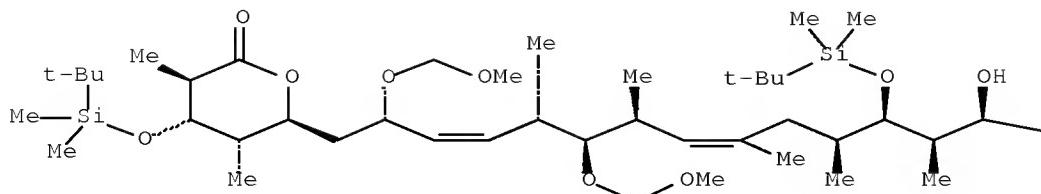
● I⁻

BR



4
STEPS
→

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PAGE 1-B



^{CD}
YIELD 91%

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

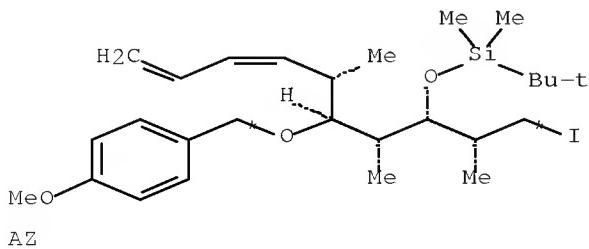
STAGE(2)

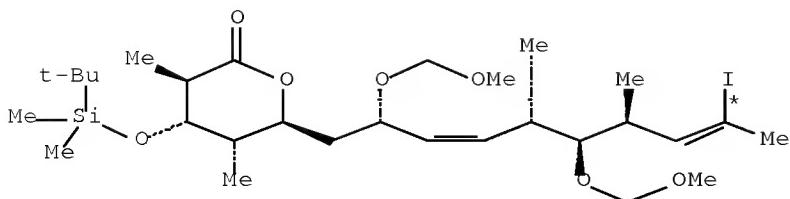
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

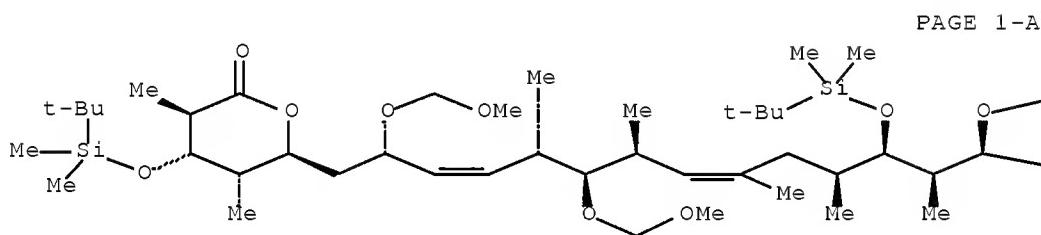
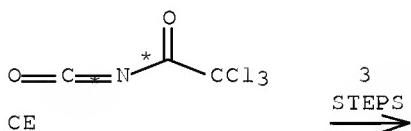
RX(89) OF 178 COMPOSED OF RX(21), RX(22), RX(23)

RX(89) AZ + CB + CE ==> CF

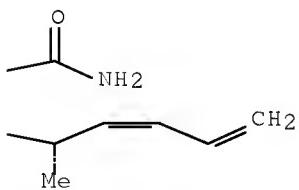




CB



PAGE 1-B



^{CF}
YIELD 92%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0

Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
 RGT BG 84-58-2 DDQ
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

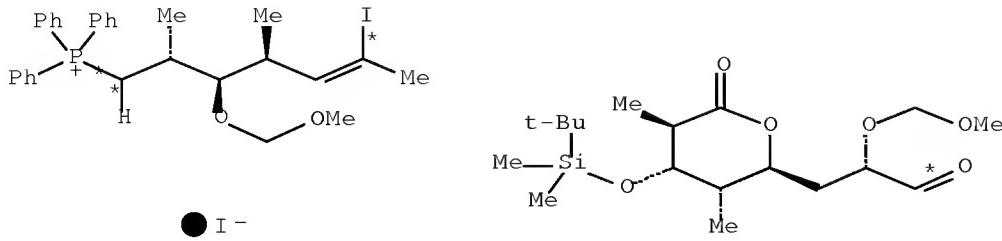
RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)
 SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
 CON 30 minutes, room temperature

STAGE(2)
 RGT CG 1344-28-1 Al₂O₃
 CON 4 hours, room temperature

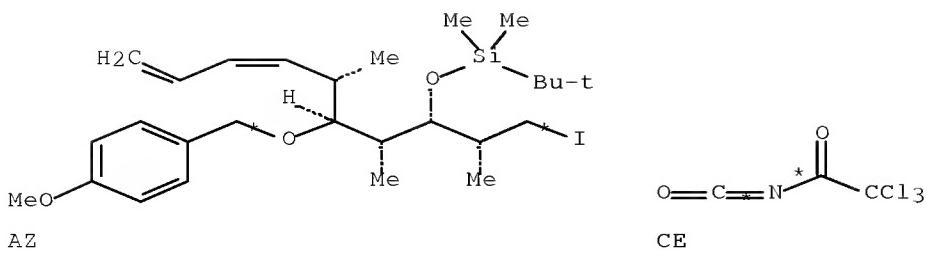
PRO CF 852049-61-7

RX(91) OF 178 COMPOSED OF RX(20), RX(21), RX(22), RX(23)
 RX(91) BR + CA + AZ + CE ==> CF

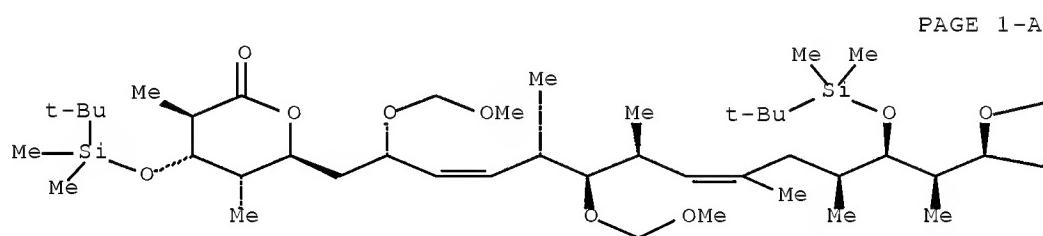


BR

CA



4
 STEPS

^{CF}
YIELD 92%

RX(20) RCT BR 850211-72-2

STAGE (1)
RGT BU 1070-89-9 (Me₃Si)₂N.Na

SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

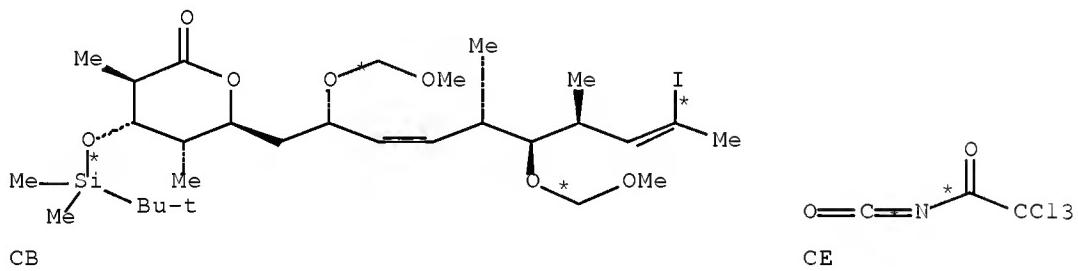
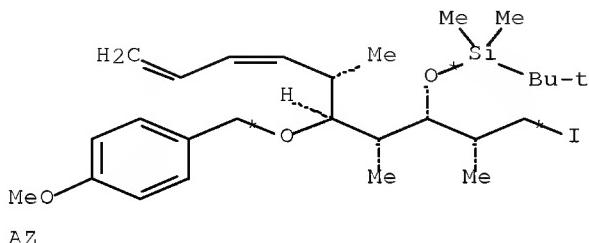
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE (2)

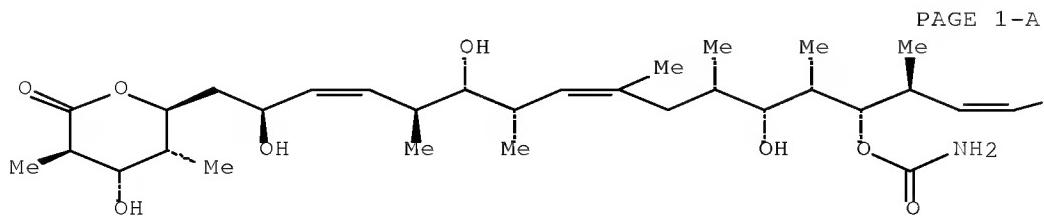
RGT CG 1344-28-1 Al2O3
 CON 4 hours, room temperature

PRO CF 852049-61-7

RX(93) OF 178 COMPOSED OF RX(21), RX(22), RX(23), RX(24)
 RX(93) AZ + CB + CE ==> CI



4
STEPS
→





CI
YIELD 95%

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyldiemethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDO
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
 CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

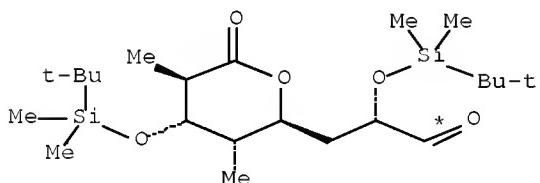
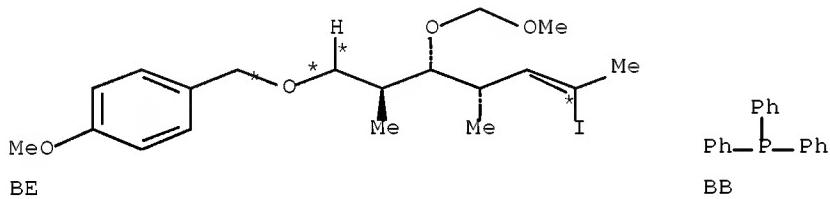
RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

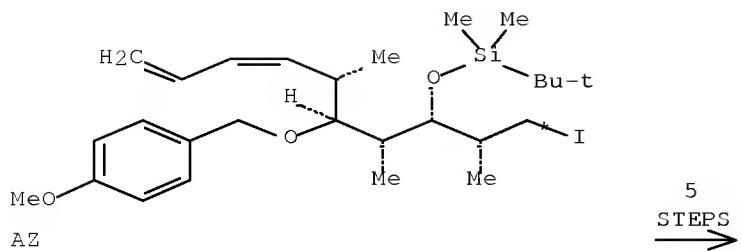
STAGE(2)

RGT BH 144-55-8 NaHCO3
CON room temperature

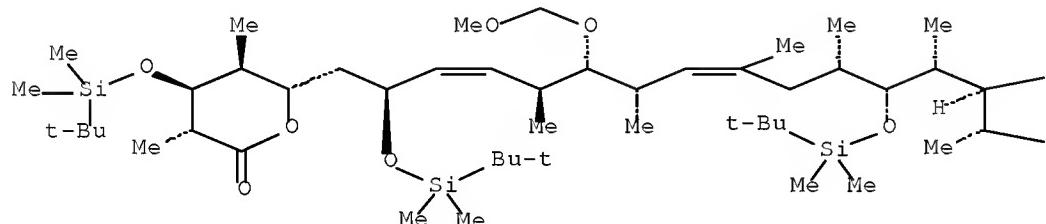
PRO CI 127943-53-7

RX(136) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(16), RX(17)
RX(136) BE + BB + BS + AZ ==> BV

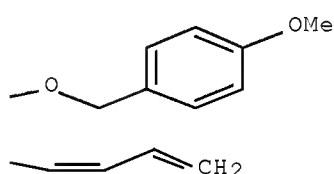




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BV
YIELD 40%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDO
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et20, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO3
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(16) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT BS 252342-51-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH4Cl
 SOL 7732-18-5 Water, 60-29-7 Et20

PRO BT 850211-74-4

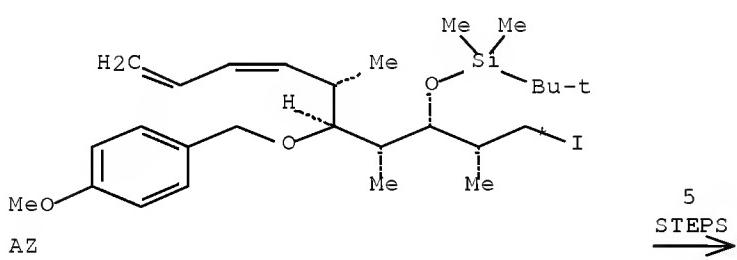
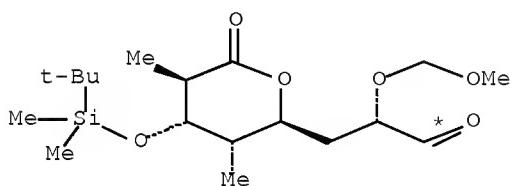
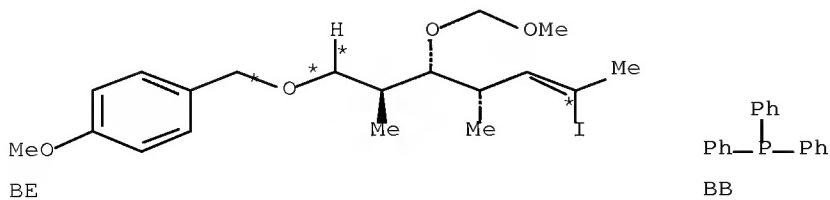
RX(17) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediyethylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et20, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

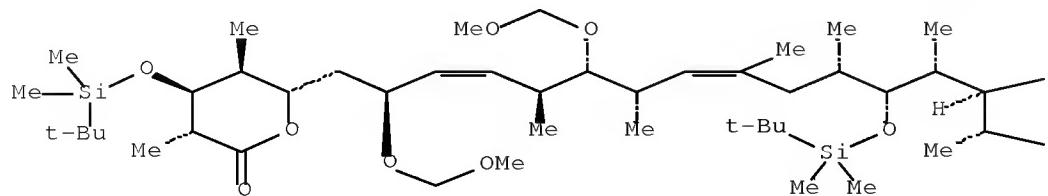
STAGE(2)
 RCT BT 850211-74-4
 RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water
 CON 20 hours, room temperature

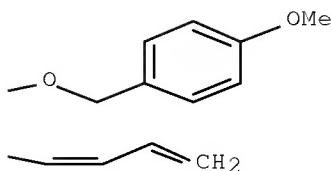
PRO BV 633293-75-1
 NTE in the dark

RX(137) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21)
 RX(137) BE + BB + CA + AZ ==> CC



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CC
YIELD 60%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C

SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

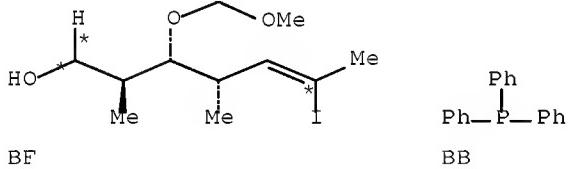
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

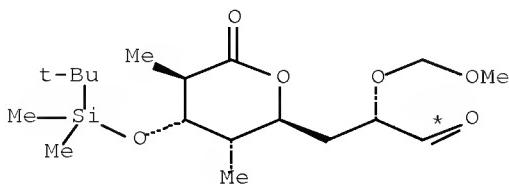
PRO CC 852049-59-3

RX(138) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22)
RX(138) BF + BB + CA + AZ ==> CD

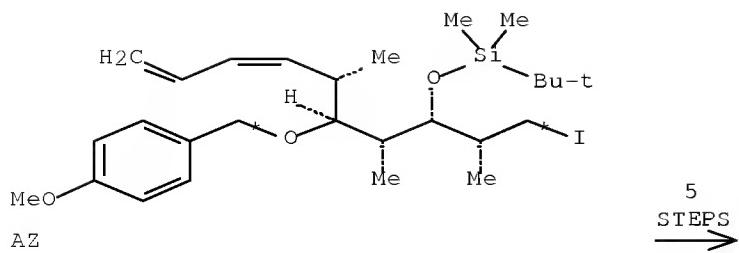


BF

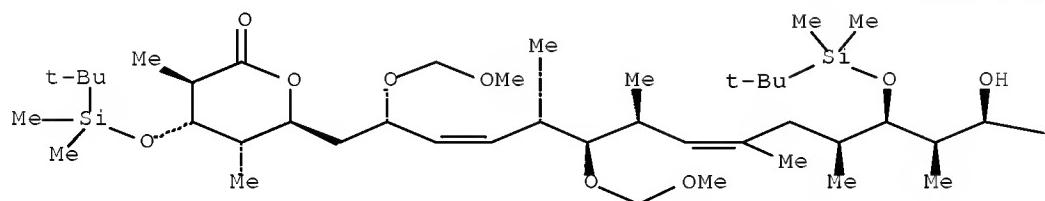
BB



CA



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PAGE 1-B



^{CD}
YIELD 91%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et2O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C → room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

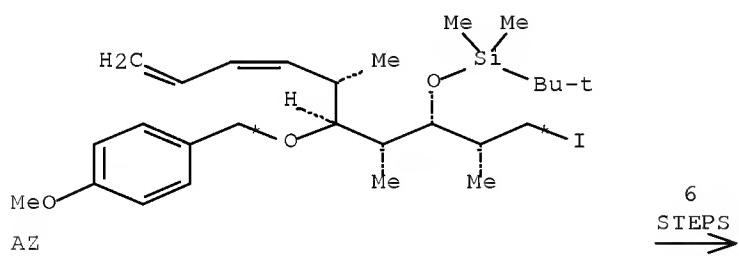
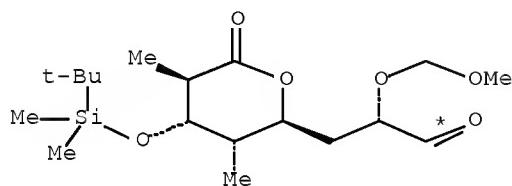
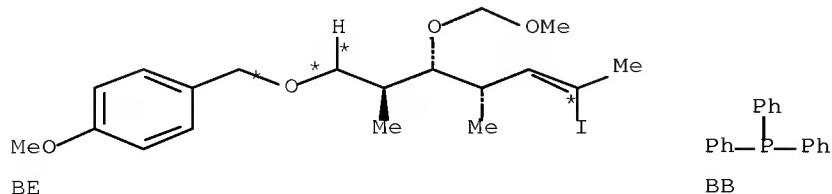
RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

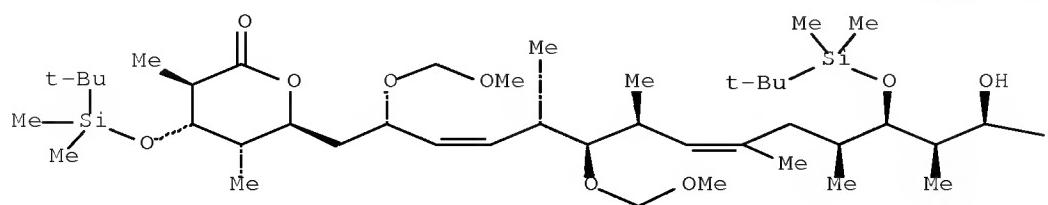
STAGE(2)
RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(139) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22)
RX(139) BE + BB + CA + AZ ==> CD



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^{CD}
YIELD 91%

RX(11) RCT BE 633294-02-7

STAGE(1)

RGT BG 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 2 hours, 0 deg C

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2

CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF

CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyethylhydroxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

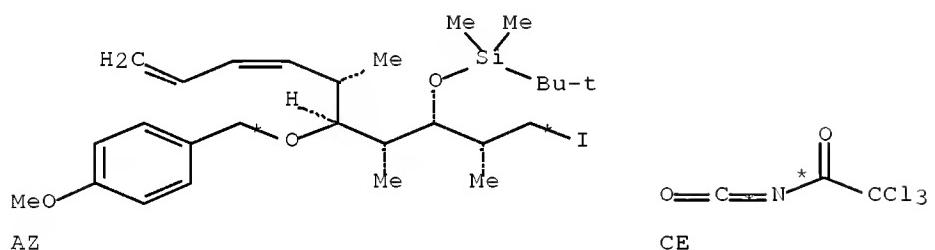
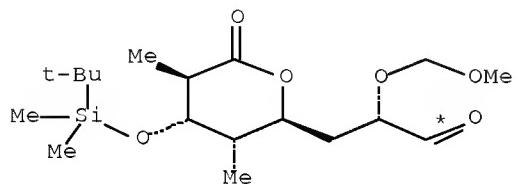
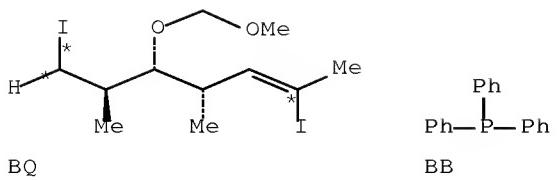
RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

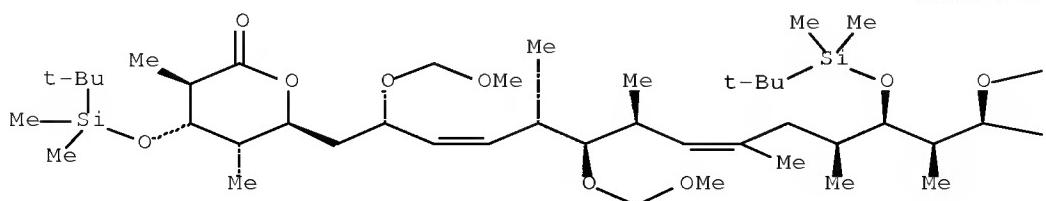
PRO CD 852049-60-6

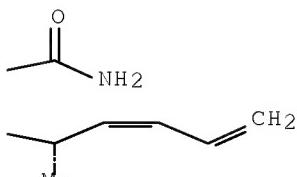
RX(140) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22), RX(23)
RX(140) BQ + BB + CA + AZ + CE ==> CF



5
STEPS
→

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^{CF}
YIELD 92%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)
 RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
 RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
 RGT BM 750545-03-0 Borate(1-),
 1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) -78 deg C
 SUBSTAGE(2) -78 deg C -> room temperature
 SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
 RCT CB 852049-58-2
 RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C → room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

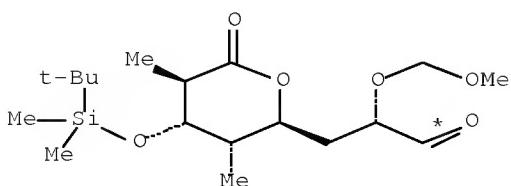
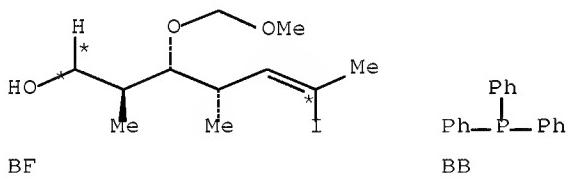
SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

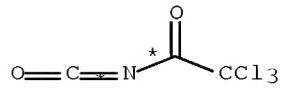
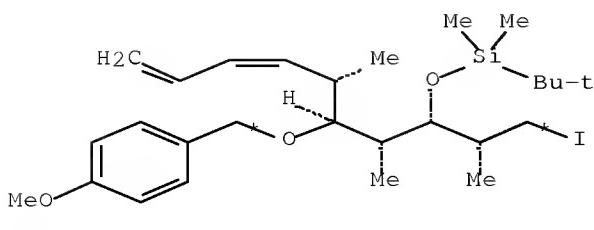
RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

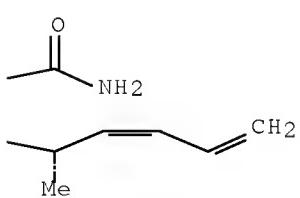
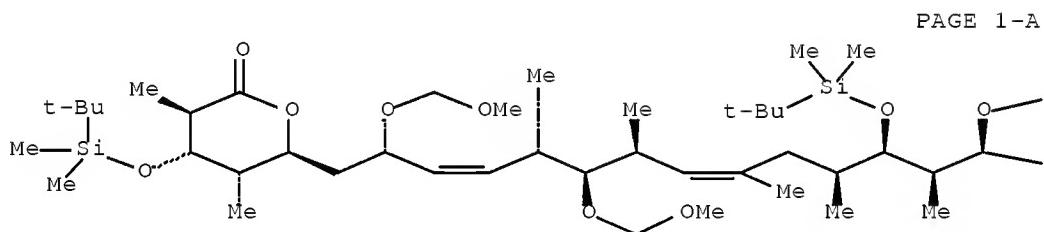
RX(141) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22), RX(23)
RX(141) BF + BB + CA + AZ + CE ==> CF



CA



6
STEPS
→



^{CF}
YIELD 92%

RX(14) RCT BF 850211-70-0

STAGE (1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh3, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et2O, 71-43-2 Benzene

CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDO
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C → room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
 CON 30 minutes, room temperature

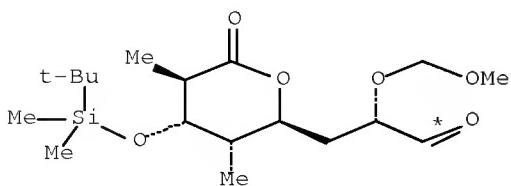
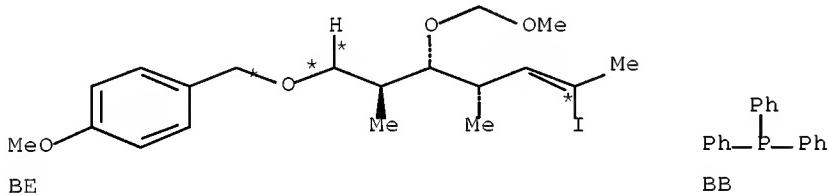
STAGE(2)

RGT CG 1344-28-1 Al₂O₃
 CON 4 hours, room temperature

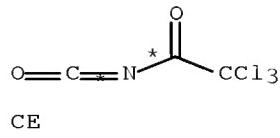
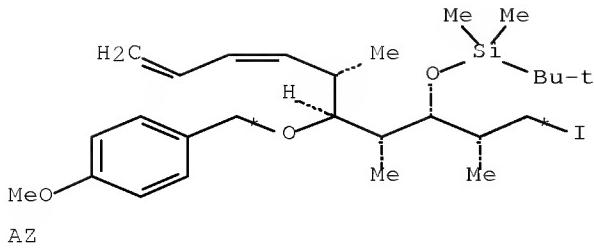
PRO CF 852049-61-7

RX(142) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22),
 RX(23)

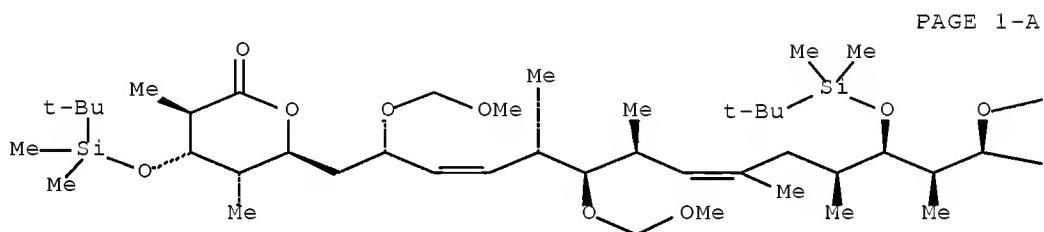
RX(142) BE + BB + CA + AZ + CE ==> CF



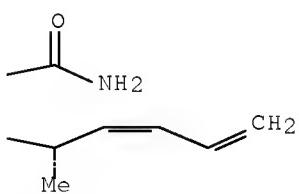
CA



7
STEPS
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PAGE 1-B



CF
YIELD 92%

RX(11) RCT BE 633294-02-7

STAGE (1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 2 hours, 0 deg C

STAGE (2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)
RGT BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C -> room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldimethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃

CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
 RGT BG 84-58-2 DDO
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON SUBSTAGE(1) 30 minutes, 0 deg C
 SUBSTAGE(2) 0 deg C \rightarrow room temperature
 SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO CD 852049-60-6

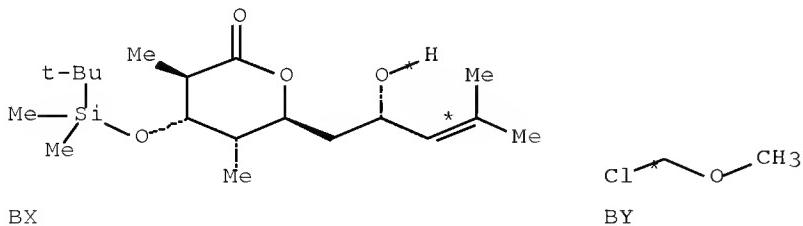
RX(23) RCT CD 852049-60-6, CE 3019-71-4

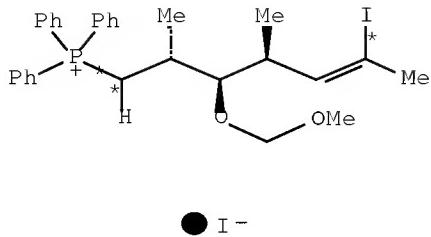
STAGE(1)
 SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
 CON 30 minutes, room temperature

STAGE(2)
 RGT CG 1344-28-1 Al₂O₃
 CON 4 hours, room temperature

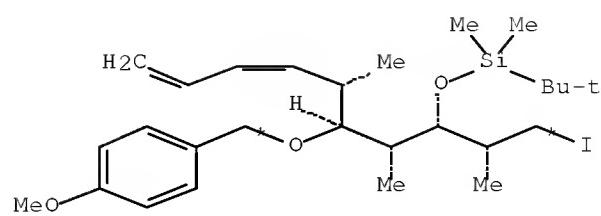
PRO CF 852049-61-7

RX(143) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22)
 RX(143) BX + BY + BR + AZ ==> CD



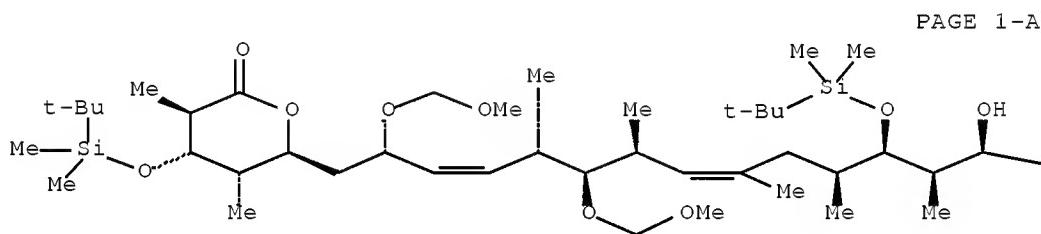


BR



AZ

5
STEPS
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PAGE 1-B



CD
YIELD 91%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE (1)

RGT H 7087-68-5 EtN(Pr-i)2
 SOL 75-09-2 CH₂C₁₂
 CON 12 hours, room temperature

STAGE (2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)
RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
SOL 75-09-2 CH2C12
CON -78 deg C

STAGE(2)
RGT BB 603-35-0 PPh3
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me3Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

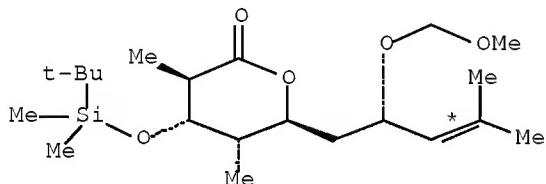
RGT BG 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C → room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

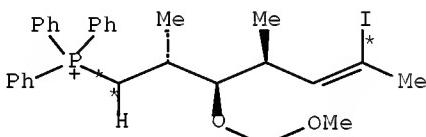
RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(144) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22), RX(23)
RX(144) BZ + BR + AZ + CE ==> CF

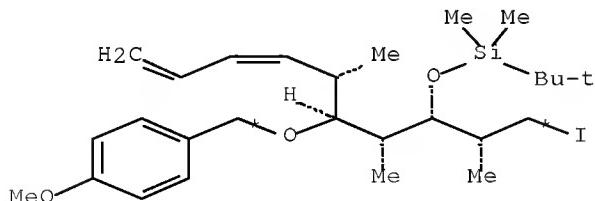


BZ

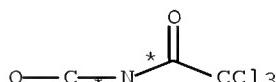


● I⁻

BR



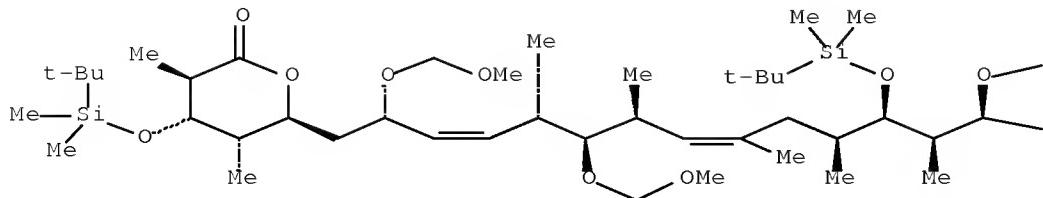
AZ



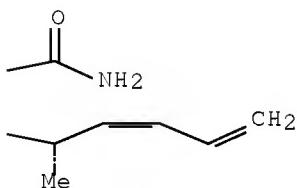
CE

5
STEPS
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PAGE 1-A



PAGE 1-B



CF
YIELD 92%

RX(19) RCT BZ 852049-62-8

STAGE (1)

RGT AM 7782-44-7 O2, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂
CON -78 deg C

STAGE (2)

RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE (1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE (2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE (3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

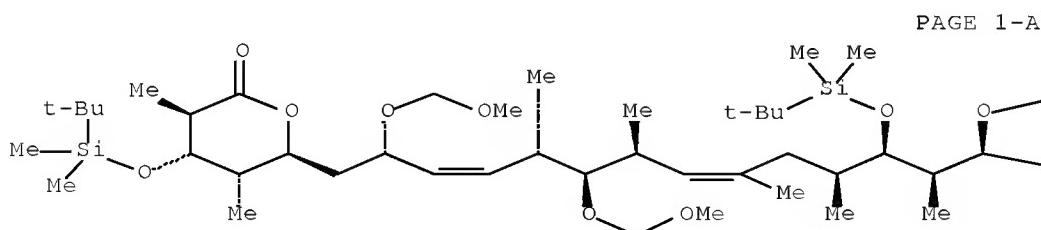
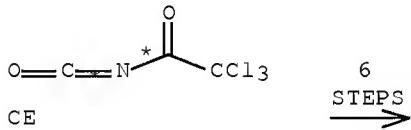
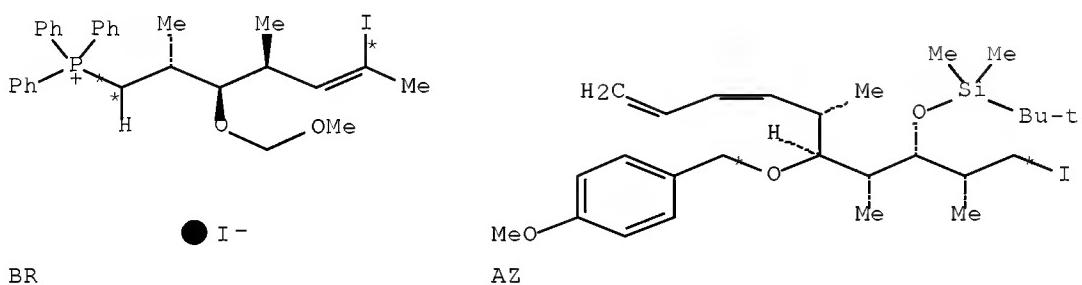
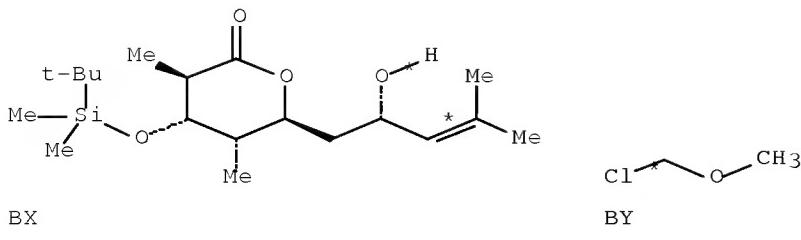
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

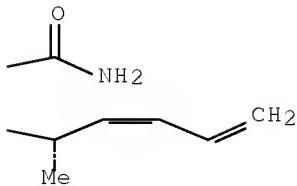
STAGE(2)

RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(145) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22), RX(23)
RX(145) BX + BY + BR + AZ + CE ==> CF





^{CF}
YIELD 92%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE(1)

RGT H 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON 12 hours, room temperature

STAGE(2)

RGT BK 7647-14-5 NaCl
SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂
CON -78 deg C

STAGE(2)

RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDO
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

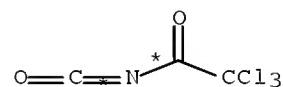
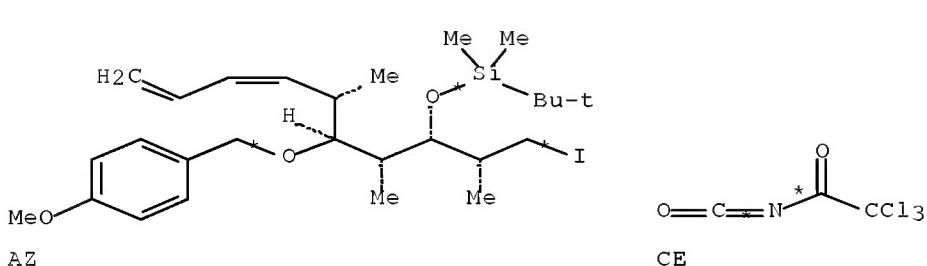
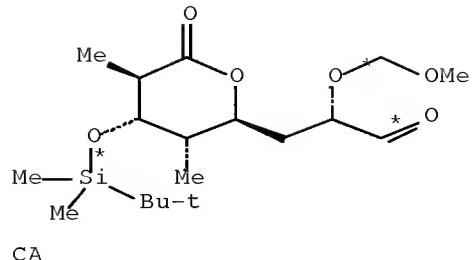
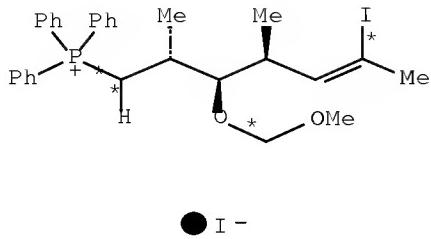
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

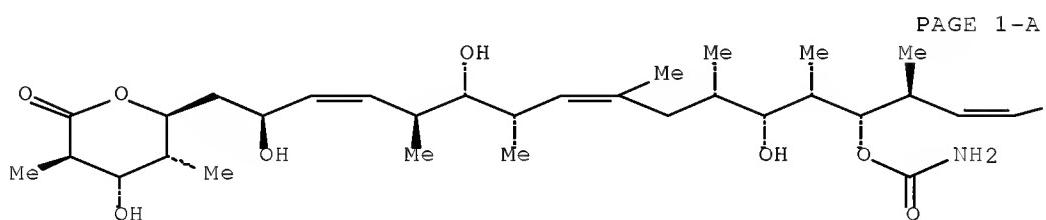
RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(146) OF 178 COMPOSED OF RX(20), RX(21), RX(22), RX(23), RX(24)
RX(146) BR + CA + AZ + CE ==> CI



5
STEPS
→



PAGE 1-B



C₁
YIELD 95%

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

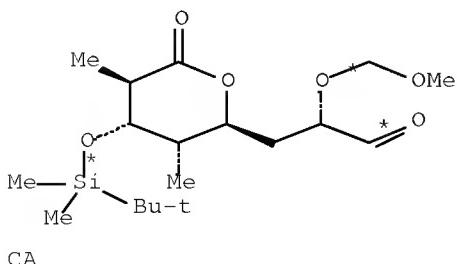
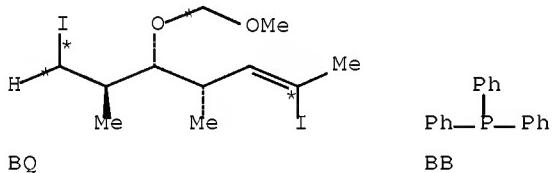
RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

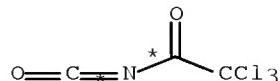
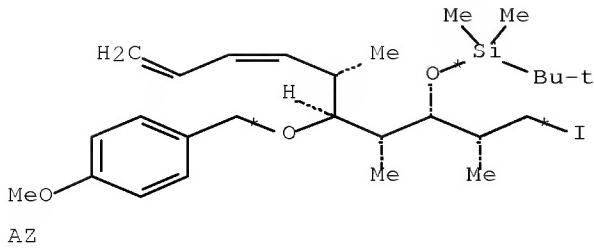
STAGE(2)

RGT BH 144-55-8 NaHCO₃
CON room temperature

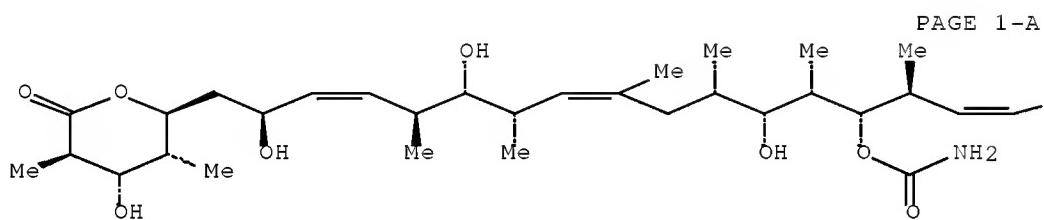
PRO CI 127943-53-7

RX(147) OF 178 COMPOSED OF RX(15), RX(20), RX(21), RX(22), RX(23), RX(24)
RX(147) BQ + BB + CA + AZ + CE ==> CI





6
STEPS
→



PAGE 1-B



CI
YIELD 95%

RX(15) RCT BQ 850211-71-1, BB 603-35-0
 PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature → 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
 RGT BU 1070-89-9 (Me3Si)2N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH4Cl
SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediylylhydromethoxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)
RGT CG 1344-28-1 Al2O3
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

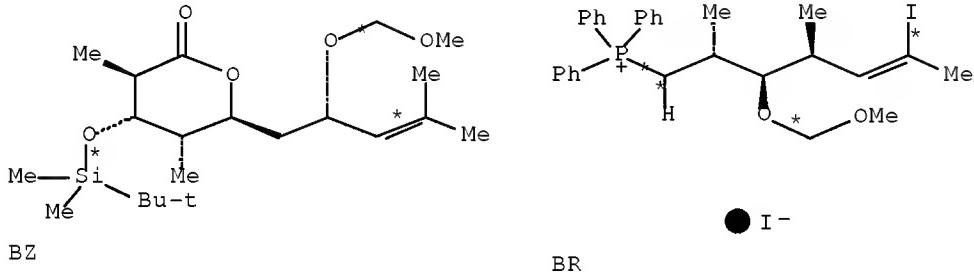
RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
CON room temperature

PRO CI 127943-53-7

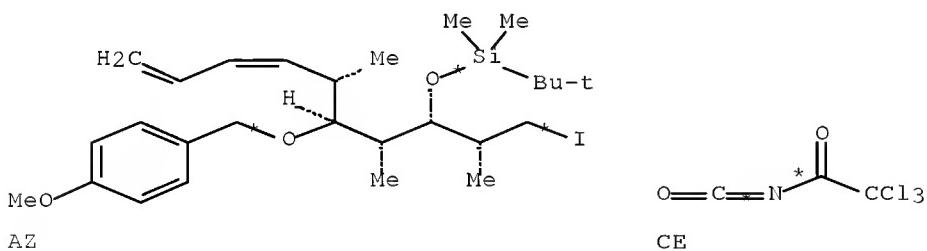
RX(148) OF 178 COMPOSED OF RX(19), RX(20), RX(21), RX(22), RX(23), RX(24)
RX(148) BZ + BR + AZ + CE ==> CI



BZ

BR

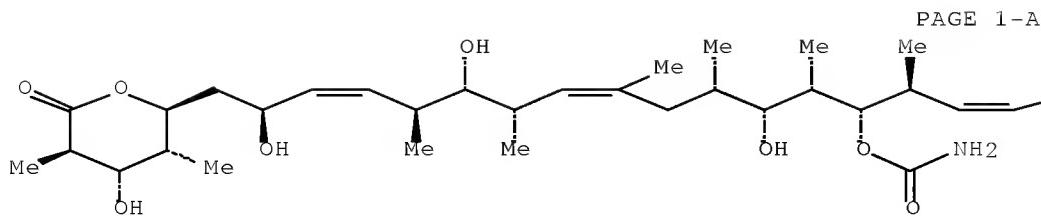
● I⁻



AZ

CE

6
STEPS
→



PAGE 1-B



^{CI}
YIELD 95%

RX(19) RCT BZ 852049-62-8

STAGE (1)

RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
 SOL 75-09-2 CH₂Cl₂
 CON -78 deg C

STAGE (2)

RGT BB 603-35-0 PPh₃
 CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE (1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE (2)

RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE (3)

RGT AJ 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE (1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyethylhydroxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3

SOL 7732-18-5 Water

CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe

CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3

CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl

SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

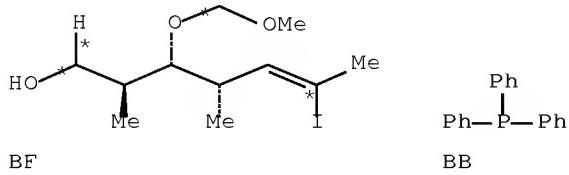
STAGE(2)

RGT BH 144-55-8 NaHCO3

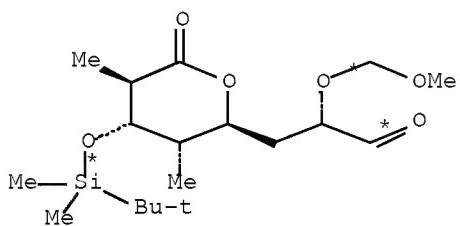
CON room temperature

PRO CI 127943-53-7

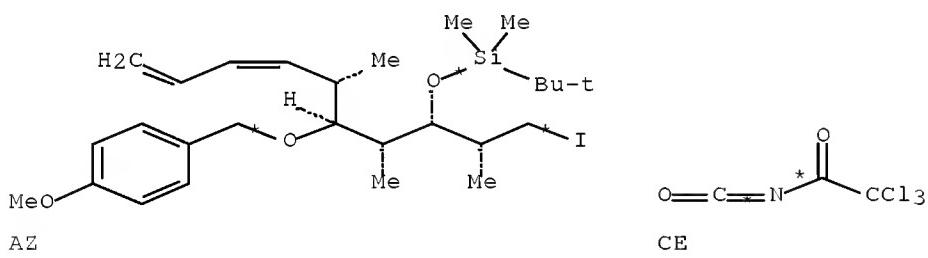
RX(149) OF 178 COMPOSED OF RX(14), RX(15), RX(20), RX(21), RX(22), RX(23),
RX(24)
RX(149) BF + BB + CA + AZ + CE ==> CI



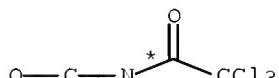
BF BB



CA

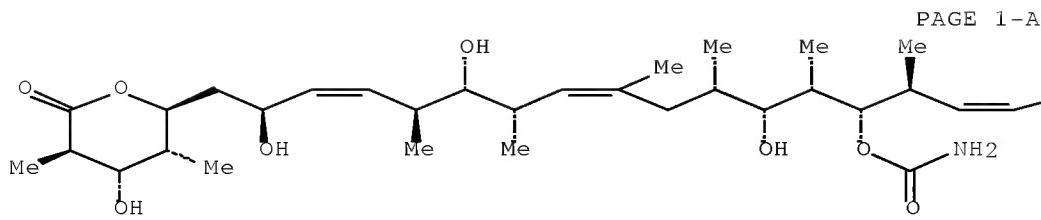


AZ



CE

7
STEPS
→



PAGE 1-B



^{CI}
YIELD 95%

RX(14) RCT BF 850211-70-0

STAGE(1)

RGT BA 7553-56-2 I2, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
 SOL 60-29-7 Et₂O, 71-43-2 Benzene
 CON SUBSTAGE(1) 0 deg C -> room temperature
 SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
 SOL 7732-18-5 Water
 CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0

PRO BR 850211-72-2
 CON SUBSTAGE(1) room temperature -> 95 deg C
 SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)

RGT BU 1070-89-9 (Me₃Si)₂N.Na
 SOL 109-99-9 THF
 CON 1 hour, -78 deg C

STAGE(2)

RCT CA 852049-57-1
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 2 hours, -78 deg C
 SUBSTAGE(2) -78 deg C -> -10 deg C
 SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)

RGT AJ 12125-02-9 NH₄Cl

SOL 7732-18-5 Water, 60-29-7 Et2O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)

RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyldihydroxy-, (T-4)-, AS 594-19-4
t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)

RCT CB 852049-58-2

RGT BW 603-32-7 Ph3As, BN 534-17-8 Cs2CO3

CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO3

SOL 7732-18-5 Water

CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH2Cl2, 108-88-3 PhMe

CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al2O3

CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl

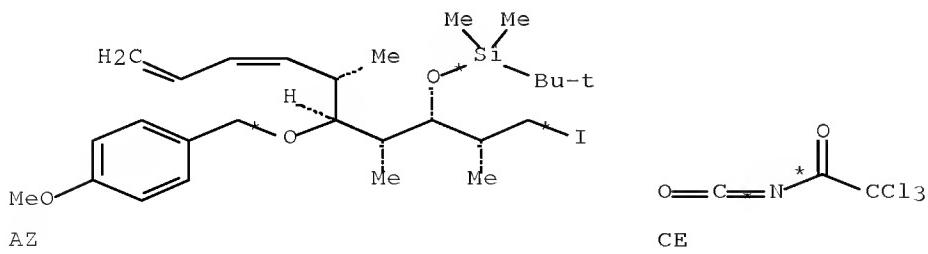
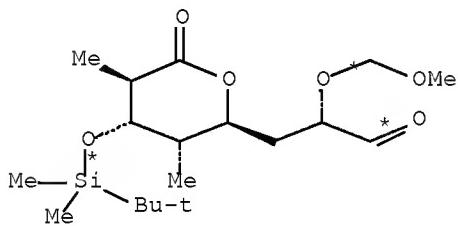
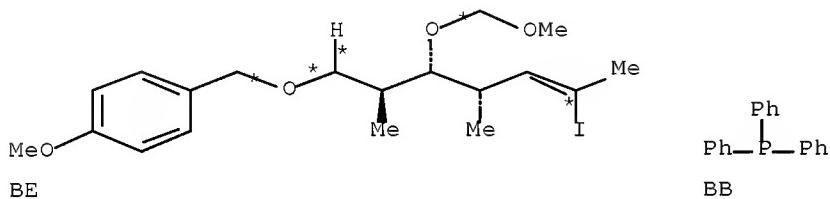
SOL 7732-18-5 Water, 67-56-1 MeOH

CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

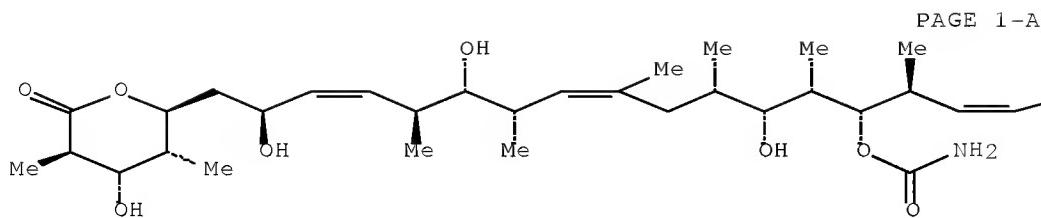
STAGE(2)
RGT BH 144-55-8 NaHCO₃
CON room temperature

PRO CI 127943-53-7

RX(150) OF 178 COMPOSED OF RX(11), RX(14), RX(15), RX(20), RX(21), RX(22),
RX(23), RX(24)
RX(150) BE + BB + CA + AZ + CE ==> CI



8
STEPS
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PAGE 1-B

$\text{CH}_2=\text{CH}_2$
CI
YIELD 95%

RX(11) RCT BE 633294-02-7

STAGE(1)

RG^T BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
CON 2 hours, 0 deg C

STAGE(2)

RG^T BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO BF 850211-70-0

RX(14) RCT BF 850211-70-0

STAGE(1)

RG^T BA 7553-56-2 I₂, BB 603-35-0 PPh₃, BC 288-32-4 1H-Imidazole
SOL 60-29-7 Et₂O, 71-43-2 Benzene
CON SUBSTAGE(1) 0 deg C → room temperature
SUBSTAGE(2) 12 hours, room temperature

STAGE(2)

RG^T BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO BQ 850211-71-1

RX(15) RCT BQ 850211-71-1, BB 603-35-0
PRO BR 850211-72-2
CON SUBSTAGE(1) room temperature -> 95 deg C
SUBSTAGE(2) 18 hours, 95 deg C

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyethylhydroxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)
RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)
RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water

CON room temperature
 PRO CD 852049-60-6
 RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)
 SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
 CON 30 minutes, room temperature

STAGE(2)
 RGT CG 1344-28-1 Al₂O₃
 CON 4 hours, room temperature

PRO CF 852049-61-7

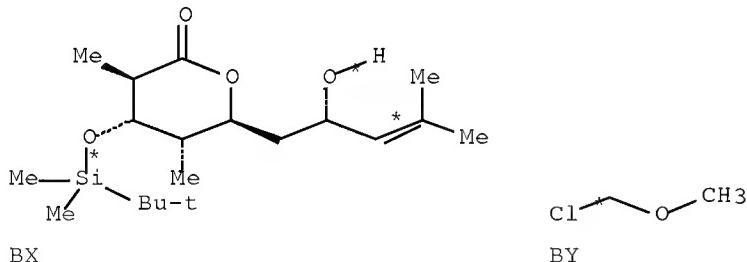
RX(24) RCT CF 852049-61-7

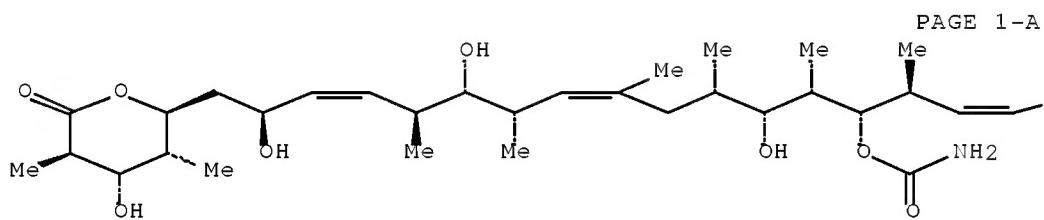
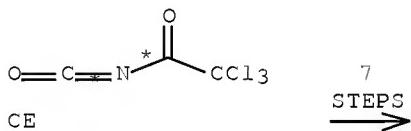
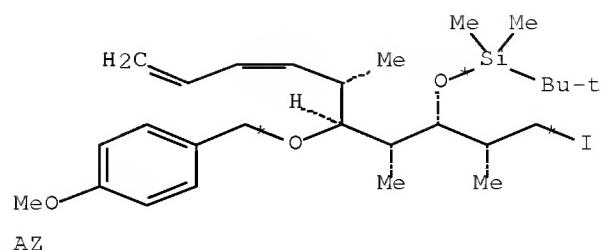
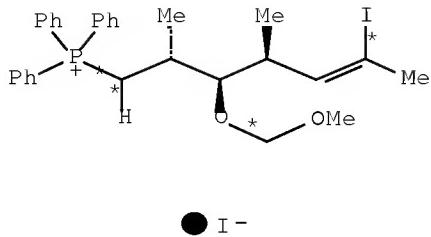
STAGE(1)
 RGT CJ 7647-01-0 HCl
 SOL 7732-18-5 Water, 67-56-1 MeOH
 CON SUBSTAGE(1) 15 minutes, room temperature
 SUBSTAGE(2) 6 hours, room temperature

STAGE(2)
 RGT BH 144-55-8 NaHCO₃
 CON room temperature

PRO CI 127943-53-7

RX(151) OF 178 COMPOSED OF RX(18), RX(19), RX(20), RX(21), RX(22), RX(23),
 RX(24)
 RX(151) BX + BY + BR + AZ + CE ==> CI





PAGE 1-B

$\text{CH}_2=\text{CH}_2$
CI
YIELD 95%

RX(18) RCT BX 256920-77-1, BY 107-30-2

STAGE (1)
RGT H 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH₂C₁₂
CON 12 hours, room temperature

STAGE (2)
RGT BK 7647-14-5 NaCl

SOL 7732-18-5 Water
CON room temperature

PRO BZ 852049-62-8

RX(19) RCT BZ 852049-62-8

STAGE(1)
RGT AM 7782-44-7 O₂, AN 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂
CON -78 deg C

STAGE(2)
RGT BB 603-35-0 PPh₃
CON 1 hour, room temperature

PRO CA 852049-57-1

RX(20) RCT BR 850211-72-2

STAGE(1)
RGT BU 1070-89-9 (Me₃Si)2N.Na
SOL 109-99-9 THF
CON 1 hour, -78 deg C

STAGE(2)
RCT CA 852049-57-1
SOL 109-99-9 THF
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> -10 deg C
SUBSTAGE(3) 2 hours, -10 deg C

STAGE(3)
RGT AJ 12125-02-9 NH₄Cl
SOL 7732-18-5 Water, 60-29-7 Et₂O

PRO CB 852049-58-2

RX(21) RCT AZ 850211-69-7

STAGE(1)
RGT BM 750545-03-0 Borate(1-),
1,5-cyclooctanediyethylhydroxy-, (T-4)-, AS 594-19-4
t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> room temperature
SUBSTAGE(3) 1 hour, room temperature

STAGE(2)
RCT CB 852049-58-2
RGT BW 603-32-7 Ph₃As, BN 534-17-8 Cs₂CO₃
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO CC 852049-59-3

RX(22) RCT CC 852049-59-3

STAGE(1)

RGT BG 84-58-2 DDQ
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON SUBSTAGE(1) 30 minutes, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 15 minutes, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CD 852049-60-6

RX(23) RCT CD 852049-60-6, CE 3019-71-4

STAGE(1)

SOL 75-09-2 CH₂Cl₂, 108-88-3 PhMe
CON 30 minutes, room temperature

STAGE(2)

RGT CG 1344-28-1 Al₂O₃
CON 4 hours, room temperature

PRO CF 852049-61-7

RX(24) RCT CF 852049-61-7

STAGE(1)

RGT CJ 7647-01-0 HCl
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 15 minutes, room temperature
SUBSTAGE(2) 6 hours, room temperature

STAGE(2)

RGT BH 144-55-8 NaHCO₃
CON room temperature

PRO CI 127943-53-7

L3 ANSWER 6 OF 9 CASREACT COPYRIGHT 2009 ACS on STN

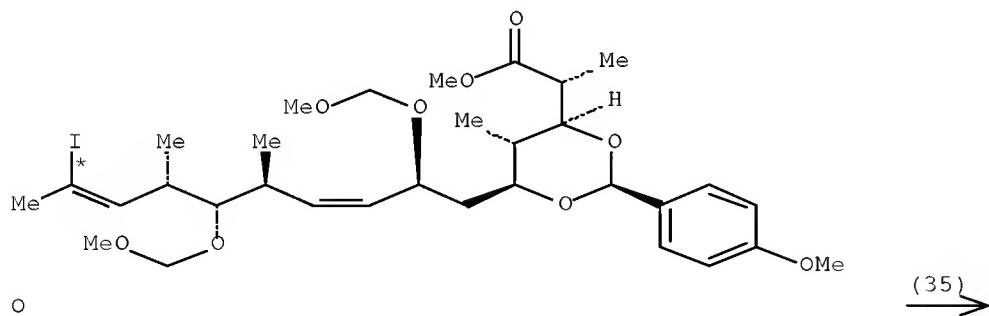
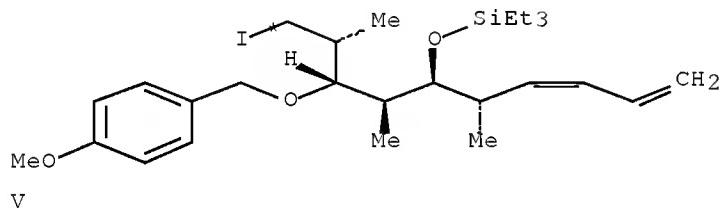
ACCESSION NUMBER: 142:481862 CASREACT Full-text
TITLE: Crotylsilane Reagents in the Synthesis of Complex
Polyketide Natural Products: Total Synthesis of
(+)-Discodermolide
AUTHOR(S): Arefolov, Alexander; Panek, James S.
CORPORATE SOURCE: Department of Chemistry and Center for Chemical
Methodology and Library Development, Metcalf Center
for Science and Engineering, Boston University,
Boston, 02215, USA
SOURCE: Journal of the American Chemical Society (2005),
127(15), 5596-5603
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

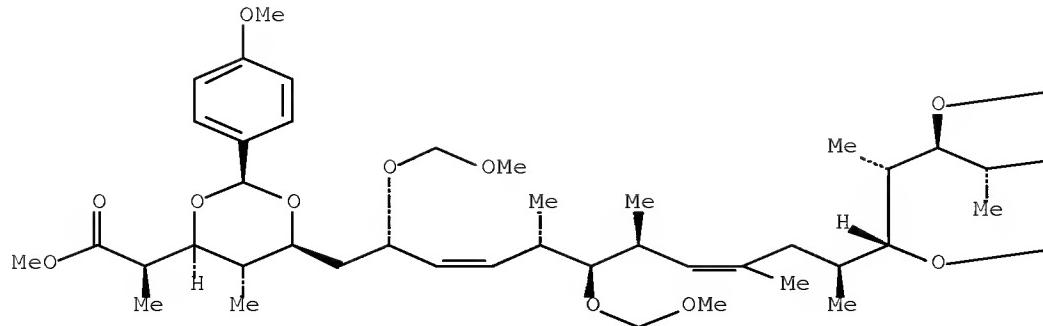
AB An efficient, highly convergent stereocontrolled synthesis of (+)-discodermolide (I) has been achieved with 2.1% overall yield (27 steps longest linear sequence). The absolute stereochem. of the C1-C6 (II; PMP = C₆H₄OMe-4), C7-C14 (III; TBS = SiMe₂CMe₃), and C15-C24 (IV; PMB = CH₂C₆H₄OMe-4) subunits was introduced using asym. crotylation methodol. Key elements of the synthesis include the use of hydrozirconation-cross-coupling methodol. for the construction of C13-C14 (Z)-olefin, acetate aldol reaction to construct the C6-C7 bond and install the C7 stereocenter with high levels of 1,5-anti stereoinduction, and the use of palladium-mediated sp₂-sp₃ cross-coupling reaction to join the advanced fragments, which assembled the carbon framework of discodermolide.

REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(35) OF 576 ...V + O ==> DJ...

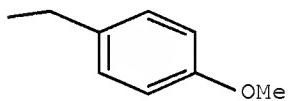


PAGE 1-A



PAGE 1-B

—SiEt₃



D_J
YIELD 82%

RX(35) RCT V 216669-69-1

STAGE (1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE (2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE (3)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE (4)

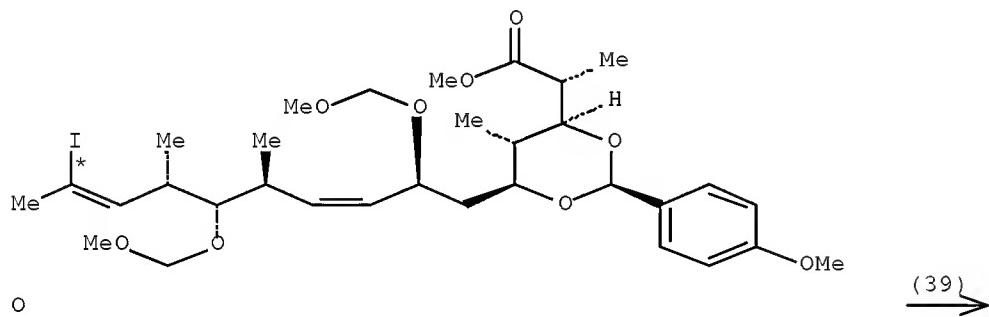
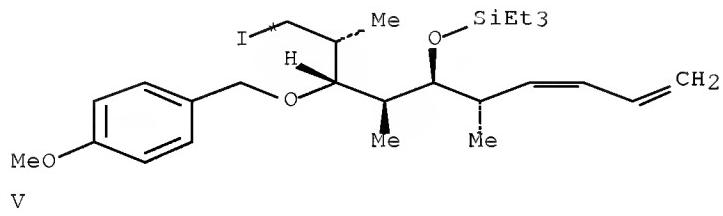
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C → room temperature
SUBSTAGE(3) 6 hours, room temperature

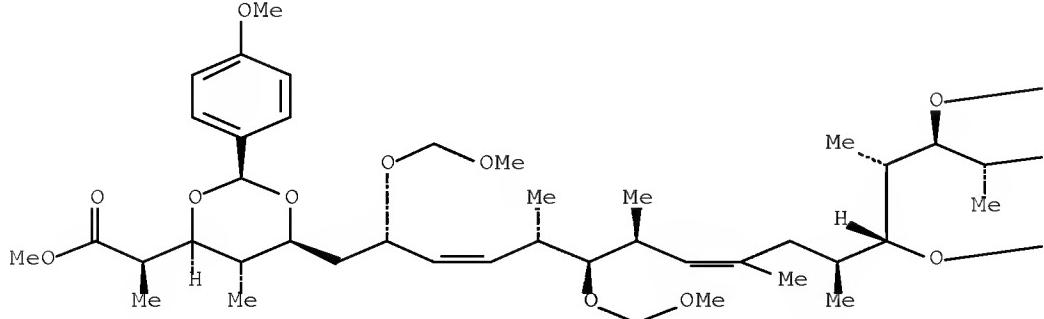
STAGE(5)
SOL 7732-18-5 Water
CON room temperature

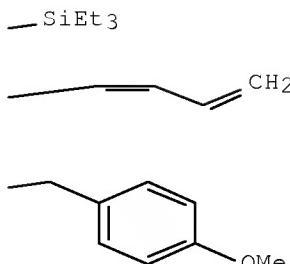
PRO DJ 851889-85-5
NTE last stage quench

RX(39) OF 576 V + O ==> DJ



PAGE 1-A





D_J
YIELD 82%

RX(39) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 3 minutes, -78 deg C

STAGE(3)

RGT DO 38050-71-4 9-BBN-OMe
SOL 110-54-3 Hexane
CON -78 deg C

STAGE(4)

SOL 109-99-9 THF
CON SUBSTAGE(1) 10 minutes, -78 deg C
SUBSTAGE(2) 1 hour, -78 deg C -> room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

STAGE(6)

RGT DP 20398-06-5 Tl(OEt)₃
CON room temperature

STAGE(7)

RCT O 851889-66-2
SOL 68-12-2 DMF
CON room temperature

STAGE(8)

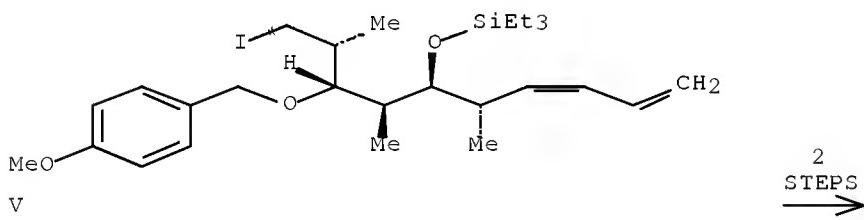
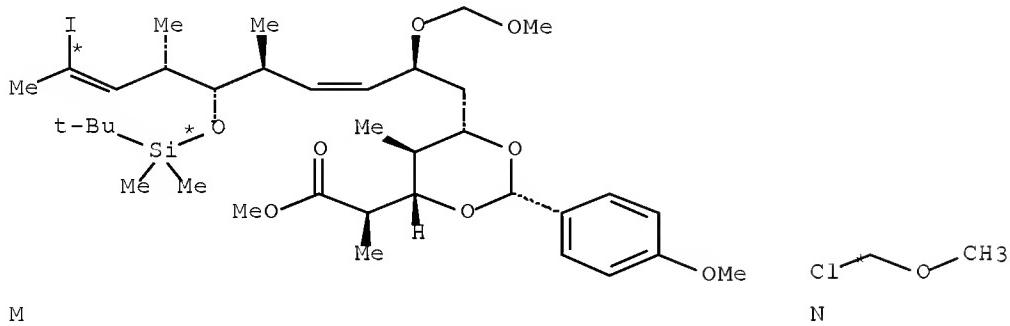
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,

(SP-4-2)-
CON 14 hours, room temperature

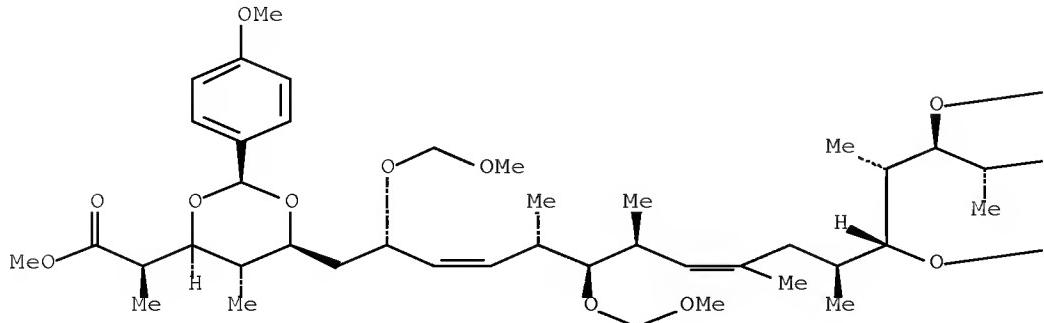
STAGE (9)
SOL 7732-18-5 Water
CON room temperature

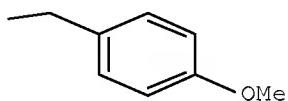
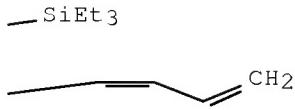
PRO DJ 851889-85-5
NTE fifth stage quench

RX(41) OF 576 COMPOSED OF RX(3), RX(35)
RX(41) M + N + V ==> DJ



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D_J
YIELD 82%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGD D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

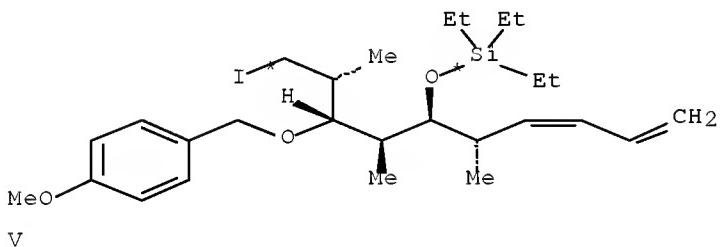
STAGE(5)

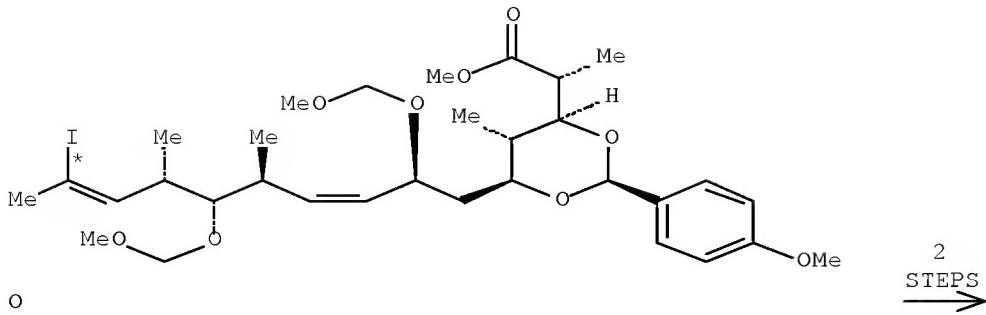
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5

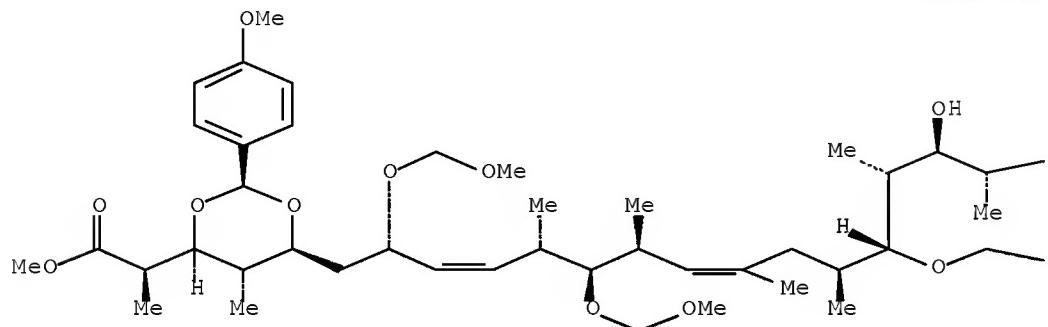
NTE last stage quench

RX(75) OF 576 COMPOSED OF RX(35), RX(36)
RX(75) V + O ==> G

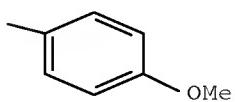




PAGE 1-A



PAGE 1-B



^G
YIELD 77%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

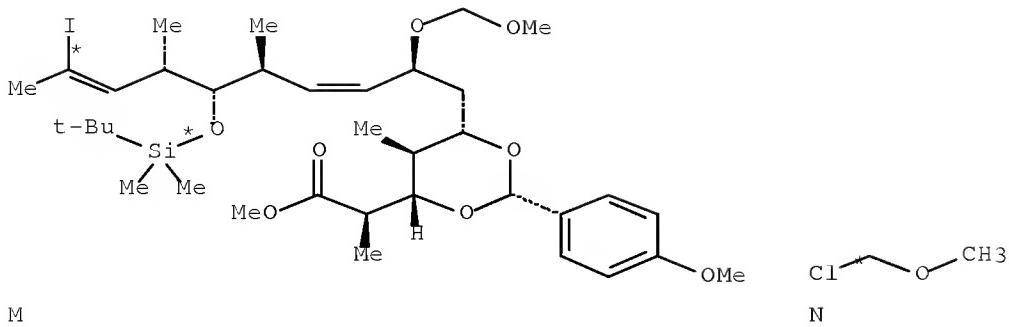
STAGE(3)

RGT AR 121-44-8 Et₃N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

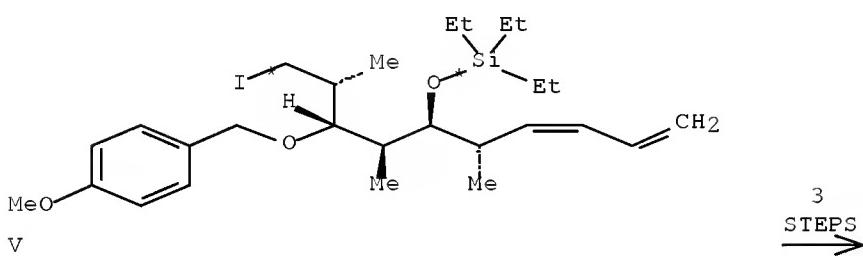
RX(81) OF 576 COMPOSED OF RX(3), RX(35), RX(36)

RX(81) M + N + V ==> G

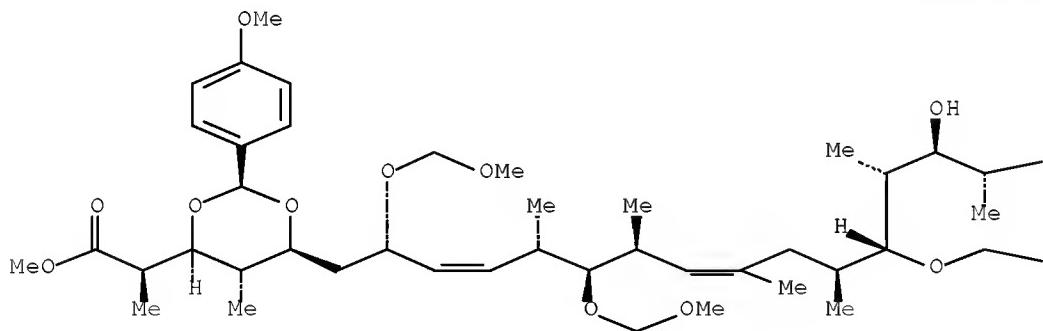


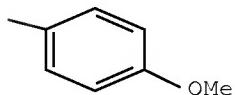
M

N



PAGE 1-A





^G
YIELD 77%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

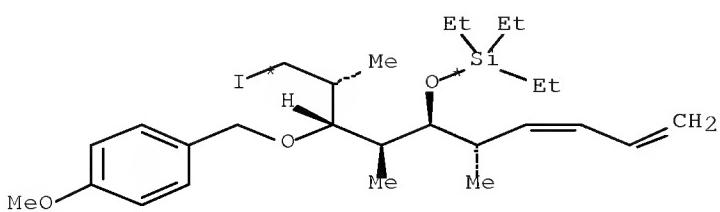
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)

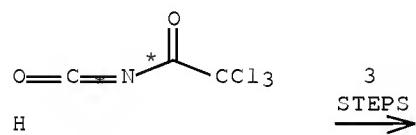
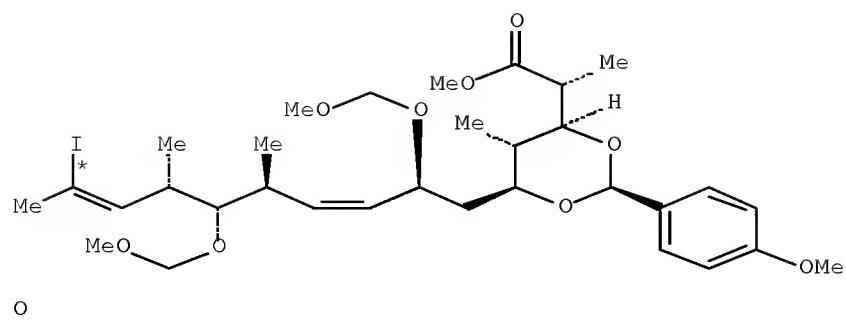
RGT AR 121-44-8 Et₃N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

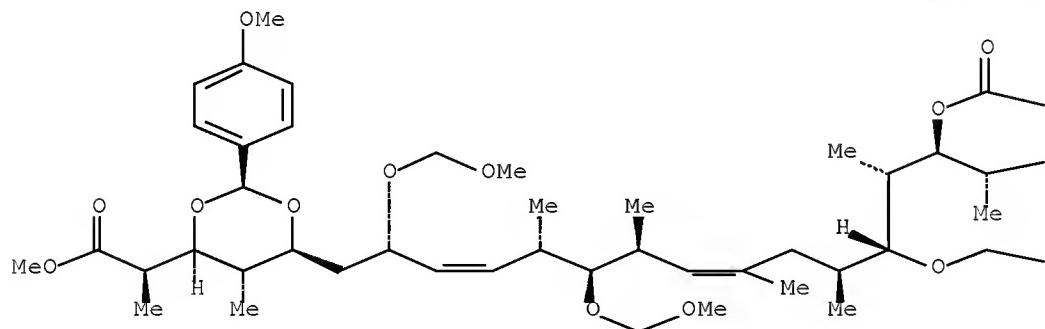
RX(150) OF 576 COMPOSED OF RX(35), RX(36), RX(2)
RX(150) V + O + H ==> I

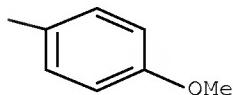
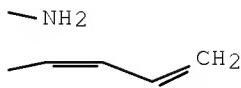


V



PAGE 1-A





I
YIELD 95%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH

CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6

NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)

RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)

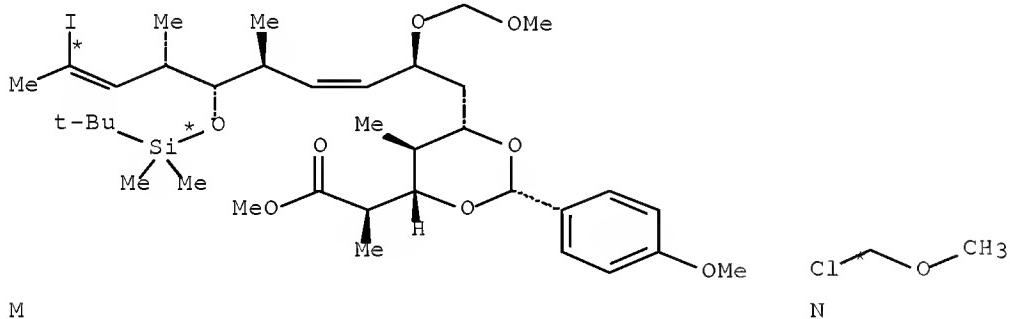
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)

RGT J 584-08-7 K₂CO₃
CON 75 minutes, room temperature

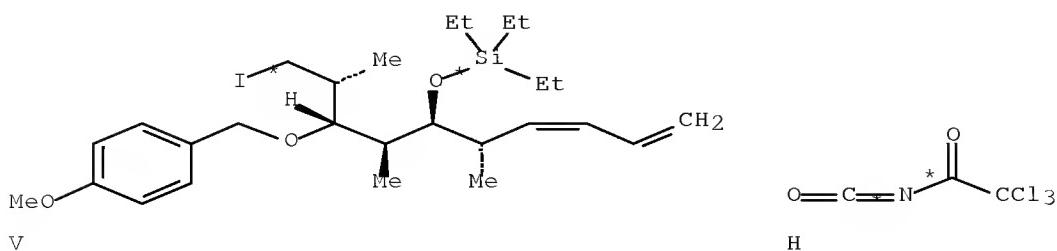
PRO I 851889-65-1

RX(151) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2)
RX(151) M + N + V + H ==> I



M

N

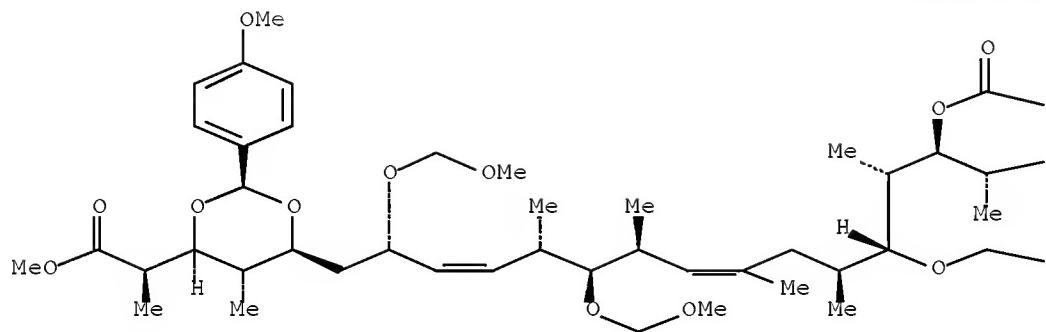


V

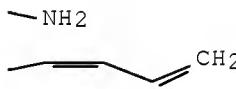
H

4
STEPS
→

PAGE 1-A



PAGE 1-B



I
YIELD 95%

RX(3) RCT M 851889-82-2

STAGE (1)
SOL 109-99-9 THF
CON room temperature

STAGE (2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F

SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5

NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6

NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)

SOL 75-09-2 CH2Cl2
CON room temperature

STAGE(2)

RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH
CON room temperature

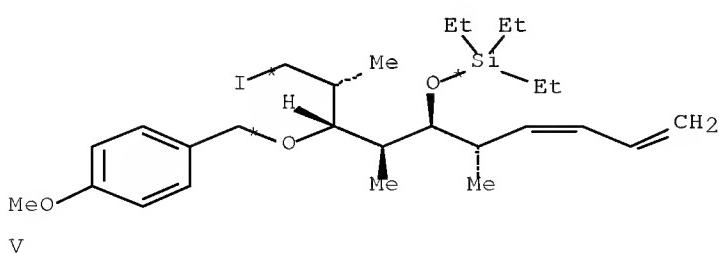
STAGE(4)

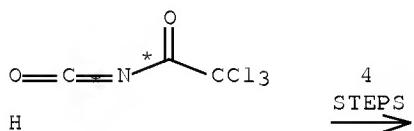
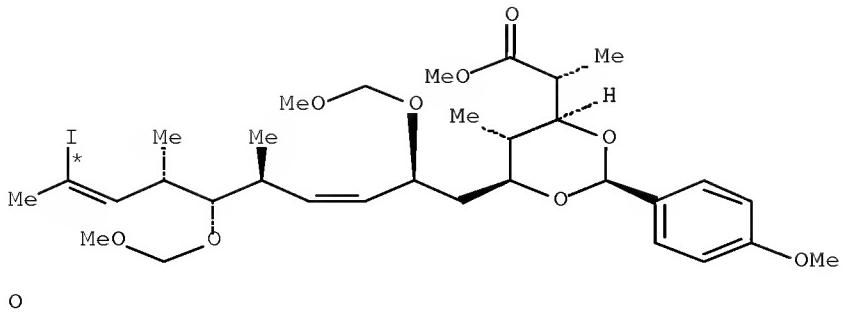
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

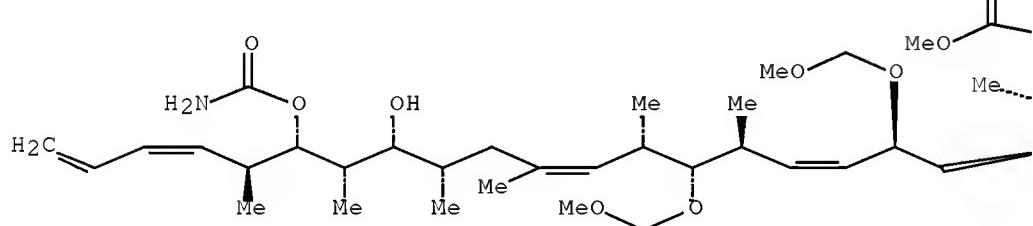
RX(154) OF 576 COMPOSED OF RX(35), RX(36), RX(2), RX(37)

RX(154) V + O + H ==> A

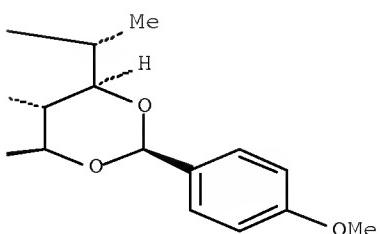




PAGE 1-A



PAGE 1-B



^A
YIELD 90%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)

RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)

SOL 67-56-1 MeOH
 CON room temperature

STAGE(4)

RGT J 584-08-7 K2CO3
 CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)

SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON room temperature

STAGE(2)

RGT D 144-55-8 NaHCO3
 CON room temperature

STAGE(3)

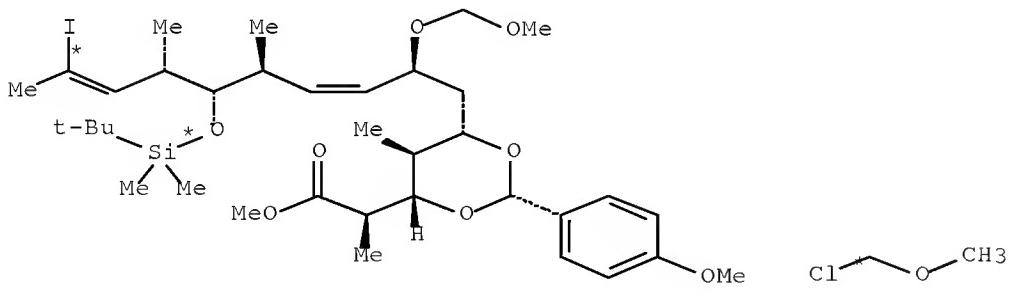
RGT DM 84-58-2 DDQ
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

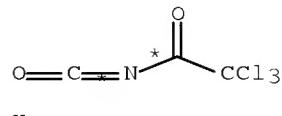
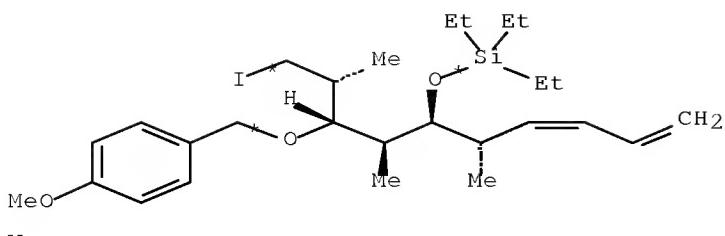
STAGE(4)

RGT DM 84-58-2 DDQ
 SOL 75-09-2 CH2Cl2
 CON 1 hour, room temperature

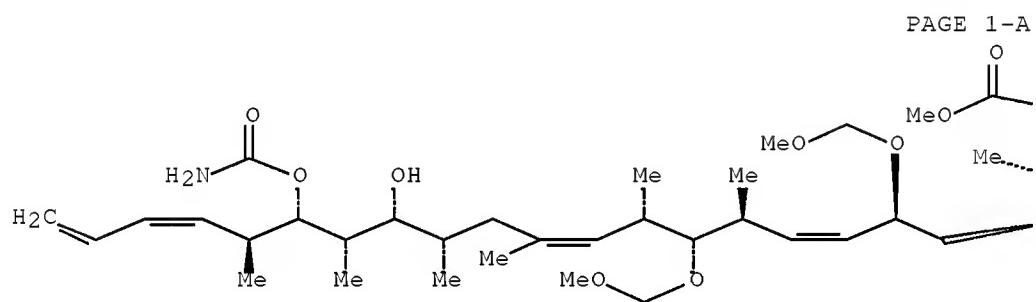
PRO A 851889-87-7

RX(157) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2), RX(37)
 RX(157) M + N + V + H ==> A

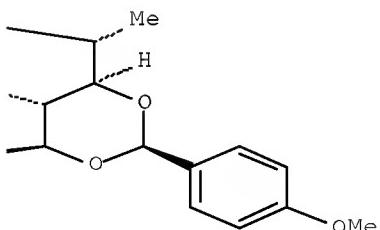




5
STEPS
→



PAGE 1-B



^A
YIELD 90%

RX(3) RCT M 851089-82-2

STAGE (1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water

CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO3
CON room temperature

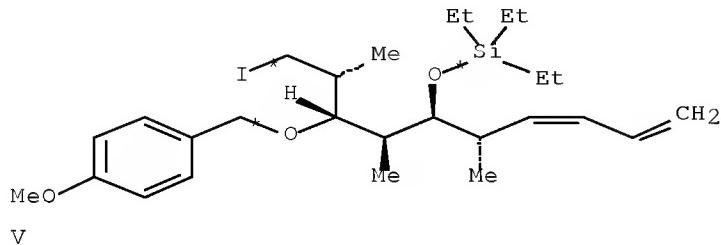
STAGE(3)
RGT DM 84-58-2 DDO
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(4)
RGT DM 84-58-2 DDO
SOL 75-09-2 CH2Cl2

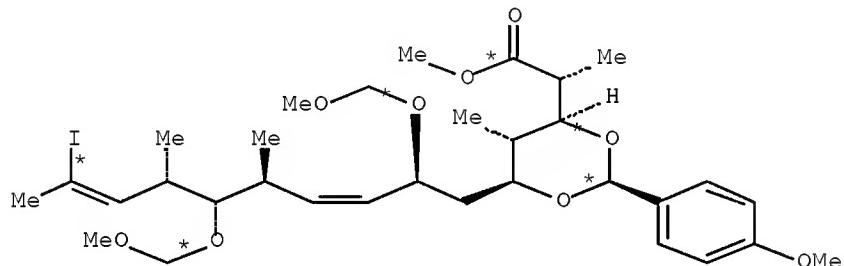
CON 1 hour, room temperature

PRO A 051889-07-7

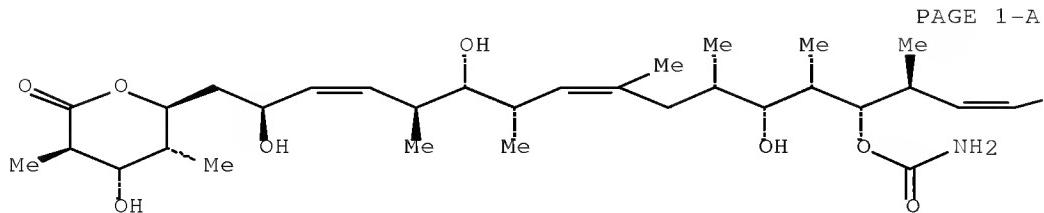
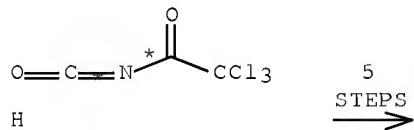
RX(313) OF 576 COMPOSED OF RX(35), RX(36), RX(2), RX(37), RX(1)
RX(313) V + O + H ==> B



V



O



C=CC CH₂

^BYIELD 69%

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
 CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
 SOL 109-66-0 Pentane
 CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -78 deg C
 SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
 CON room temperature

PRO DJ 851889-85-5

NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
 CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
 CON 1 hour, 0 deg C

STAGE(3)

RGT AR 121-44-8 Et₃N
 CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K₂CO₃
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO₃
CON room temperature

STAGE(3)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

STAGE(4)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂C₁₂
CON 1 hour, room temperature

PRO A 851889-87-7

RX(1) RCT A 851889-87-7

STAGE(1)
SOL 109-99-9 THF
CON room temperature

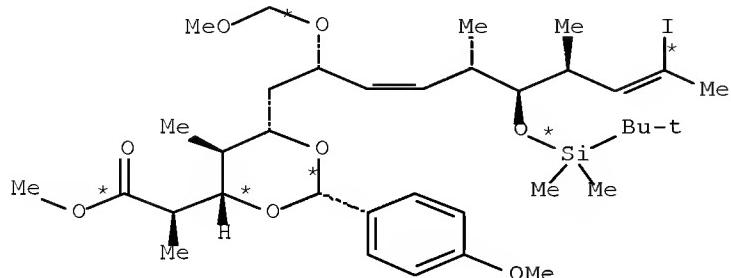
STAGE(2)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON 70 hours, room temperature

STAGE(3)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

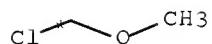
CON room temperature

PRO B 127943-53-7

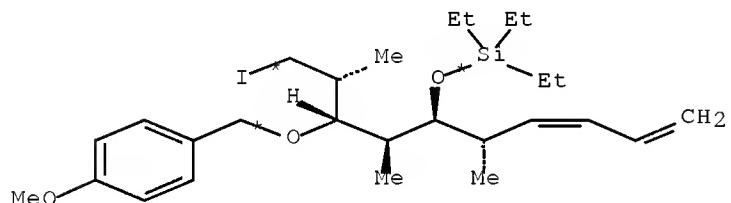
RX(314) OF 576 COMPOSED OF RX(3), RX(35), RX(36), RX(2), RX(37), RX(1)
RX(314) M + N + V + H ==> B



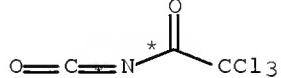
M



N

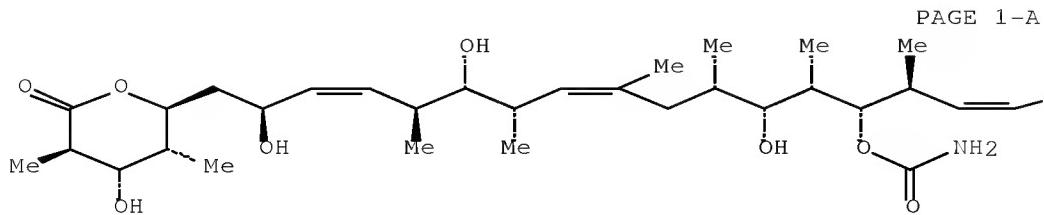


V



H

6
STEPS
→



PAGE 1-A



^B
YIELD 69%

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et₃N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K₂CO₃
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO₃
CON room temperature

STAGE(3)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

STAGE(4)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH₂Cl₂
CON 1 hour, room temperature

PRO A 851889-87-7

RX(1) RCT A 851889-87-7

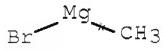
STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON 70 hours, room temperature

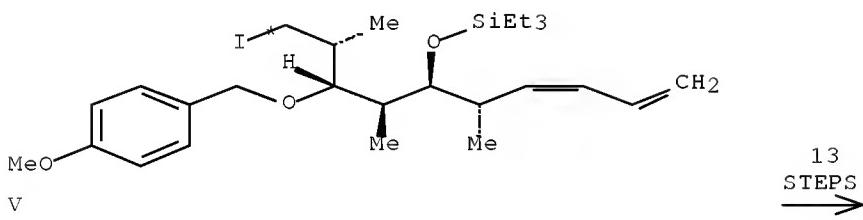
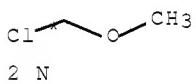
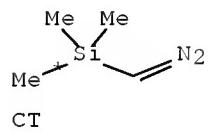
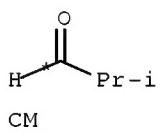
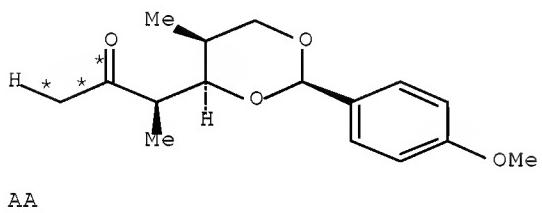
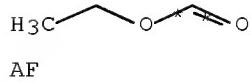
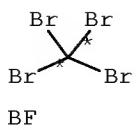
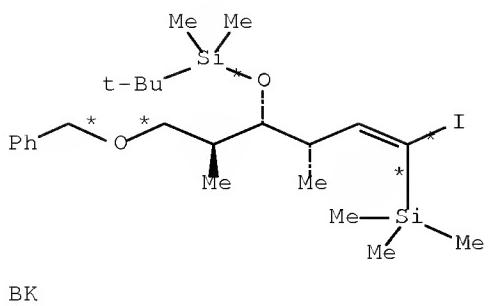
STAGE(3)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

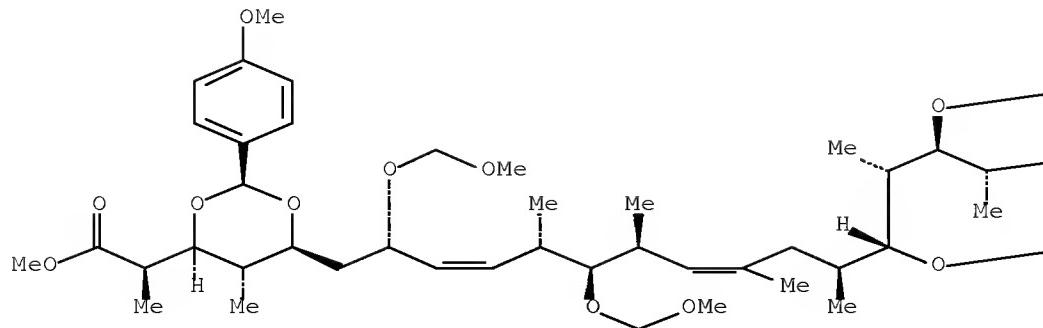
PRO B 127943-53-7

RX(382) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35)
RX(382) BM + BK + BF + AF + AA + CM + CT + 2 N +
V ==> DJ



BM





* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et₂O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F3CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe

SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et2O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7

NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)

SOL 110-54-3 Hexane

CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)

CAT 7440-05-3 Pd
CON room temperature

STAGE(4)

RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)

SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)

RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)

RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2

NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu₄N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
 SOL 7732-18-5 Water

PRO O 851889-66-2
 NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
 CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
 SOL 109-66-0 Pentane
 CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -78 deg C
 SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

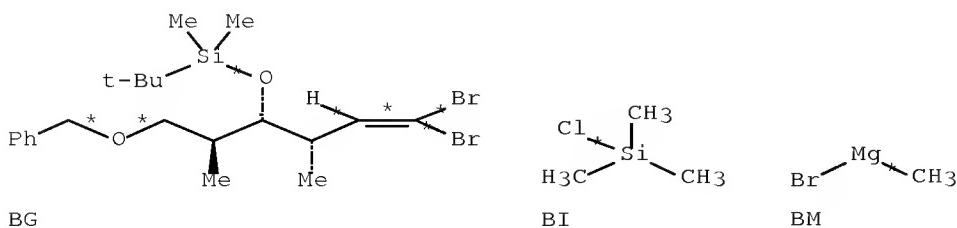
RCT O 851889-66-2
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 1 hour, 0 deg C
 SUBSTAGE(2) 0 deg C -> room temperature
 SUBSTAGE(3) 6 hours, room temperature

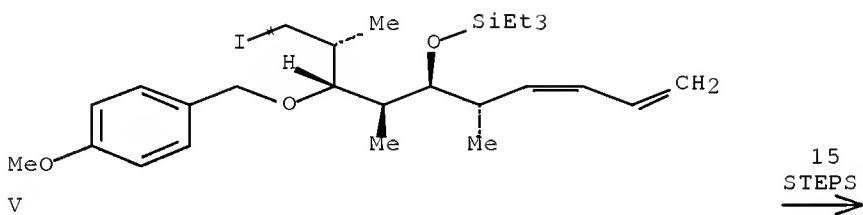
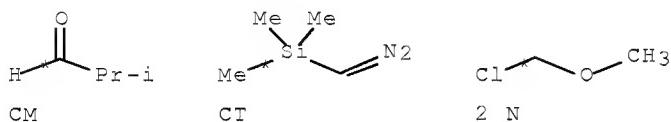
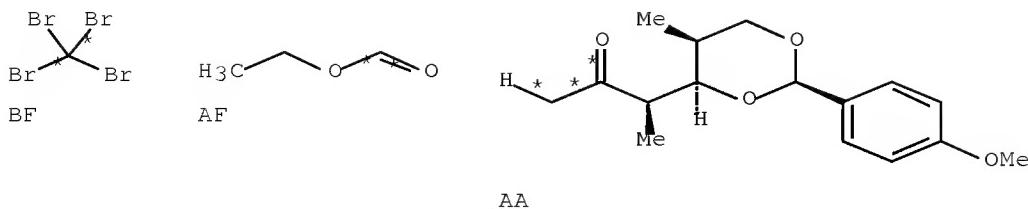
STAGE(5)

SOL 7732-18-5 Water
 CON room temperature

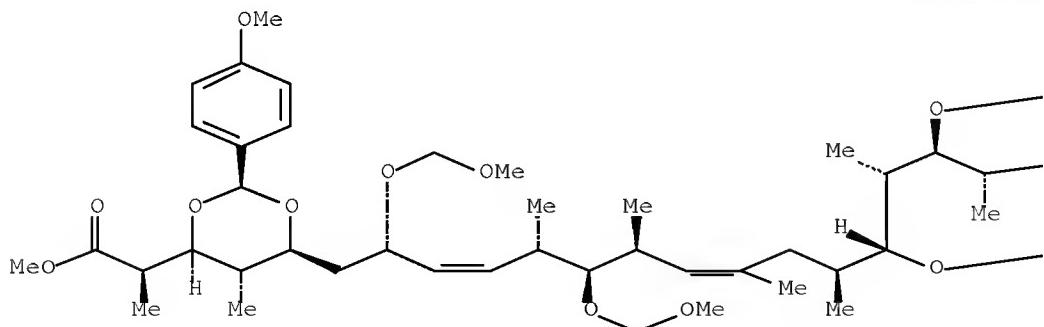
PRO DJ 851889-85-5
 NTE last stage quench

RX(398) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
 RX(6), RX(28), RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35)
 RX(398) BG + BI + BM + BF + AF + AA + CM + CT + 2 N
 + V ==> DJ





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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109-27-7

STAGE (1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT BI 75-77-4
CON 8 hours, -78 deg C -> room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)

RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)

RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂C₁₂
CON 10 minutes, 0 deg C

STAGE(2)

RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂C₁₂
CON 4 hours, 0 deg C

STAGE(3)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4

NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3

NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)

SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2C12
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)

RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF

CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water

CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2

SOL 56-23-5 CC14

CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP

CON 0 deg C

STAGE(6)

RCT N 107-30-2

CON SUBSTAGE(1) 0 deg C

SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3

SOL 7732-18-5 Water

PRO O 851889-66-2

NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O

CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi

SOL 109-66-0 Pentane

CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2

SOL 109-99-9 THF

CON SUBSTAGE(1) 5 minutes, -78 deg C

SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2

CAT 14221-01-3 Pd(PPh3)4

SOL 109-99-9 THF

CON SUBSTAGE(1) 1 hour, 0 deg C

SUBSTAGE(2) 0 deg C -> room temperature

SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

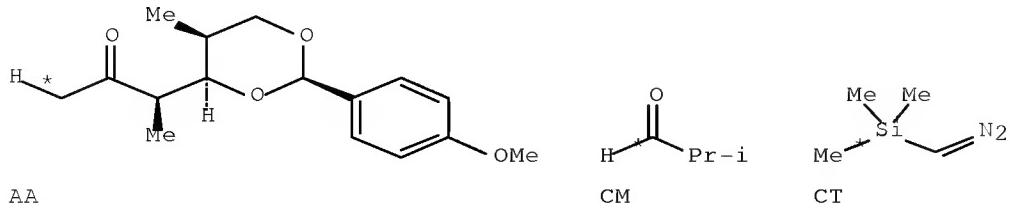
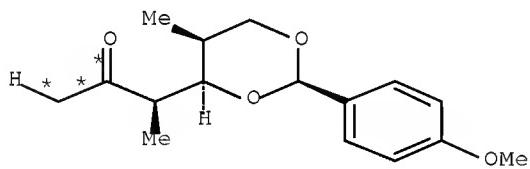
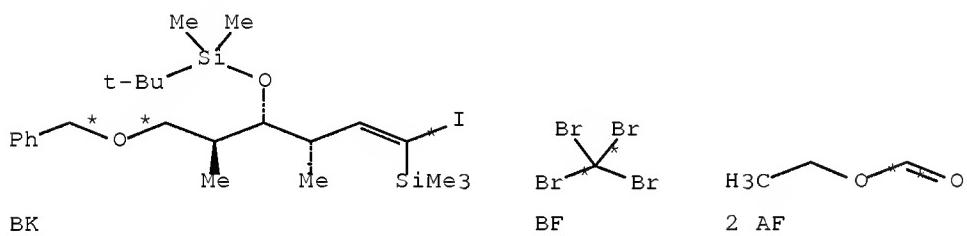
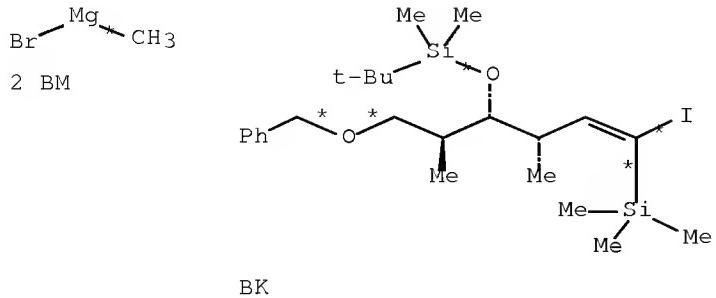
SOL 7732-18-5 Water

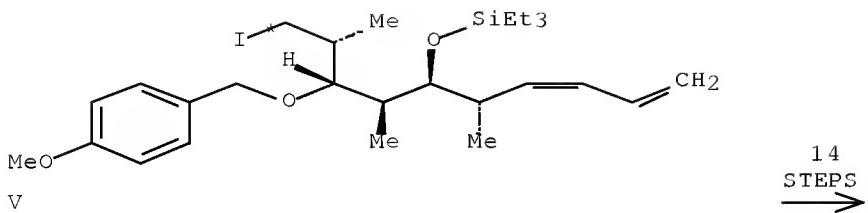
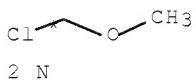
CON room temperature

PRO DJ 851889-85-5

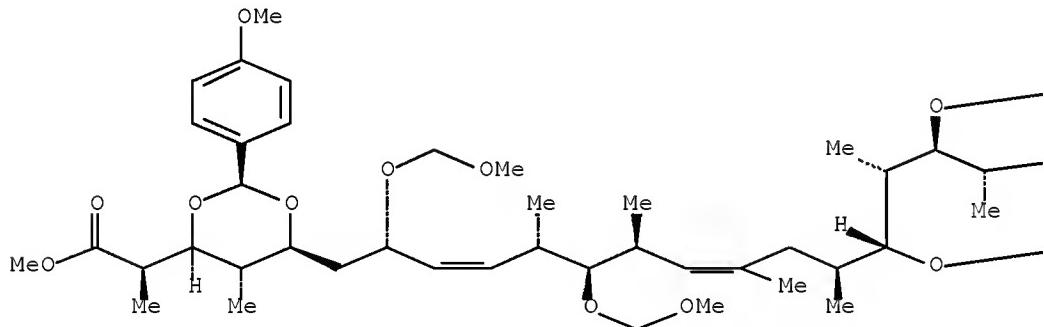
NTE last stage quench

RX(503) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
 RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3), RX(35)
 RX(503) 2 BM + 2 BK + BF + 2 AF + 2 AA + CM + CT + 2
 N + V ==> DJ





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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE (1)
 RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE (2)
 RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE (3)
 RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄

SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F3CSO3BBu2
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3
SOL 75-09-2 CH2C12
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1

NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3

NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate
SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH₂C₁₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H₂
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

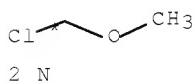
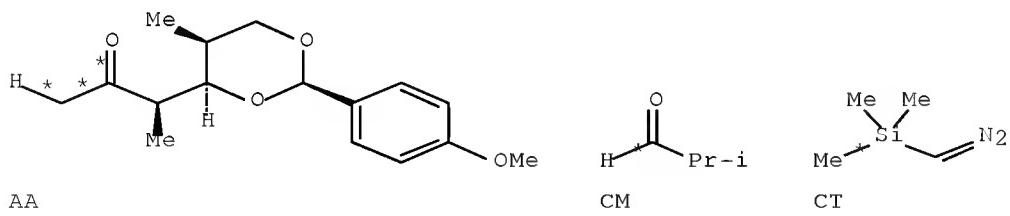
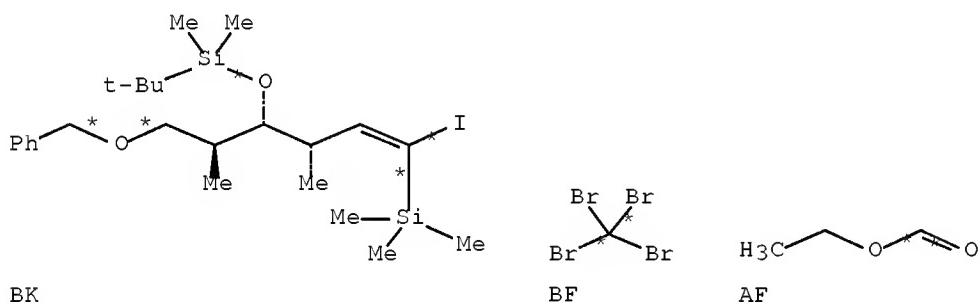
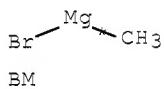
SUBSTAGE(3) 6 hours, room temperature

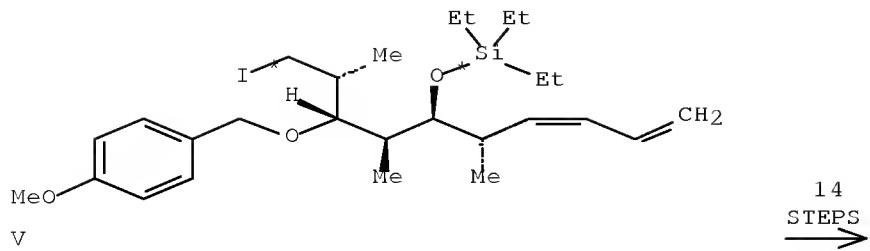
STAGE(5)

SOL 7732-18-5 Water
CON room temperature

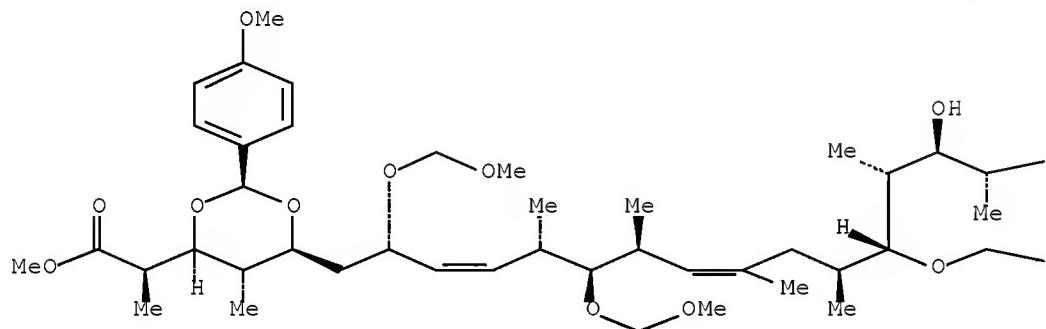
PRO DJ 851089-85-5
NTE last stage quench

RX(504) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36)
RX(504) BM + BK + BF + AF + AA + CM + CT + 2 N +
V ==> G





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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE (1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE (2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE (3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE (4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7

NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)

RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂

CON 10 minutes, 0 deg C

STAGE(2)

RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂Cl₂
CON 4 hours, 0 deg C

STAGE(3)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4

NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)

SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)

RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3

NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)

SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)

RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)

RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)

RCT AG 444109-23-3

SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)

SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)

RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1

NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)

RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3

NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature

STAGE(2)

RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H₂
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu₄N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE (2)

CAT 104-15-4 TsOH
 CON 1 hour, 0 deg C

STAGE (3)

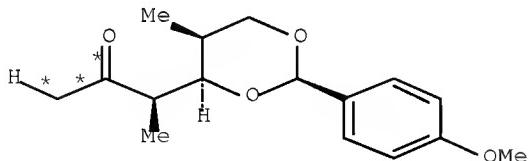
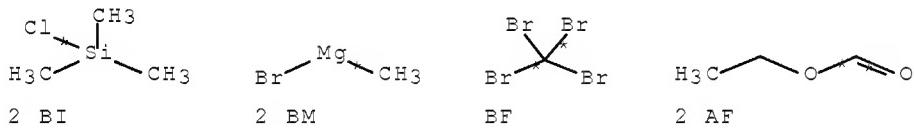
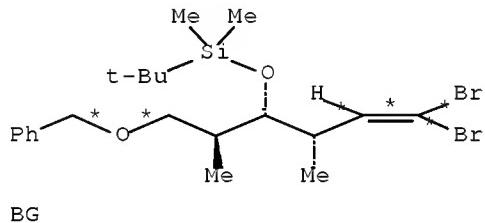
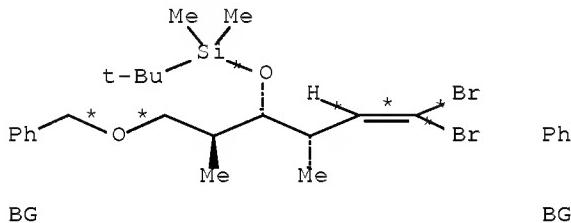
RGT AR 121-44-8 Et3N
 CON 0 deg C

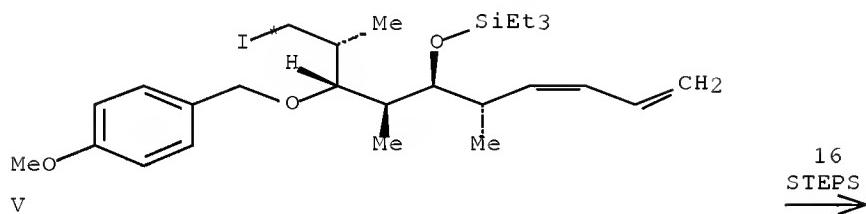
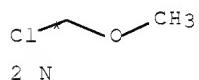
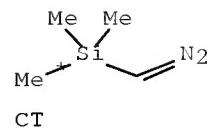
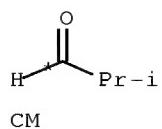
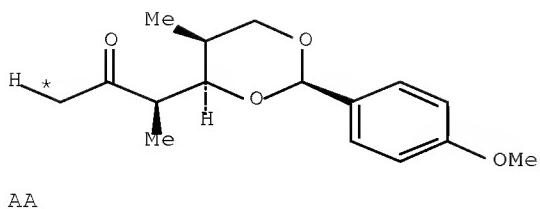
PRO G 851889-86-6

NTE last stage quench

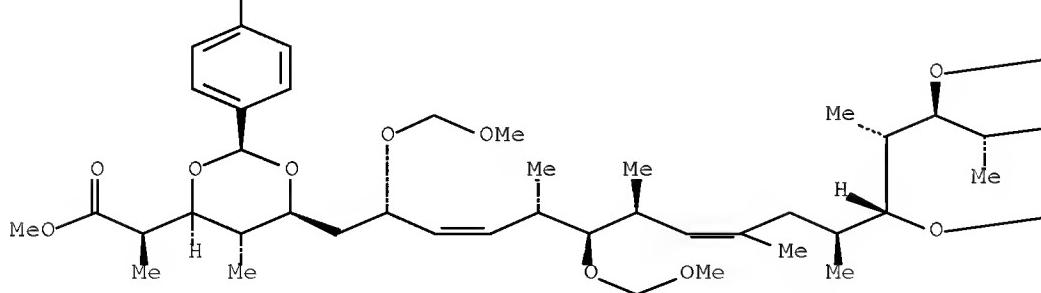
RX(507) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
 RX(6), RX(28), RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3),
 RX(35)

RX(507) 2 BG + 2 BI + 2 BM + BF + 2 AF + 2 AA + CM +
 CT + 2 N + V ==> DJ





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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109-27-7

STAGE(1)

SOL 109-99-9 THF

CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT BI 75-77-4
CON 8 hours, -78 deg C -> room temperature

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)
RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)
RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂C₁₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂C₁₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate
SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH₂C₁₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H₂
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

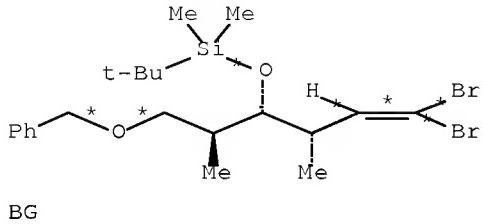
STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

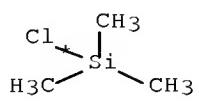
PRO DJ 851889-85-5
NTE last stage quench

RX(508) OF 576 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(18),
RX(6), RX(28), RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35),
RX(36)

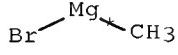
RX(508) BG + BI + BM + BF + AF + AA + CM + CT + 2 N
+ V ==> G



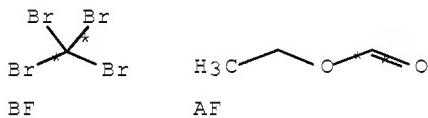
BG



BI

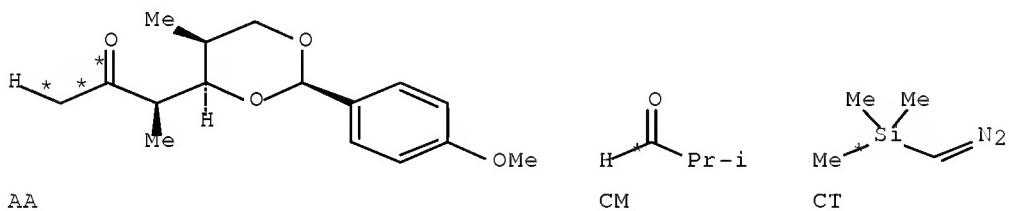


BM



BF

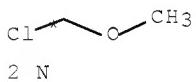
AF



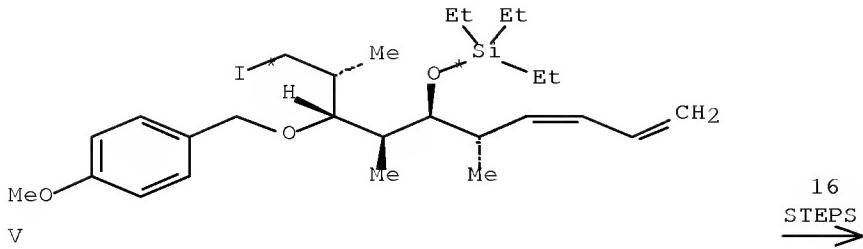
AA

CM

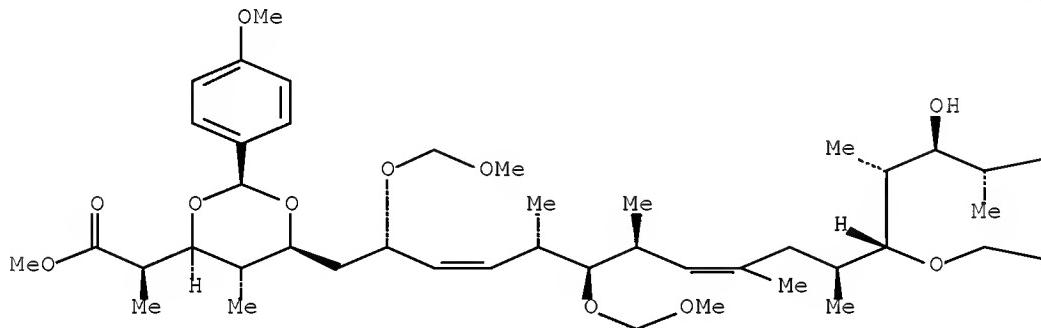
CT



2 N



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(13) RCT BG 444109-27-7

STAGE(1)

SOL 109-99-9 THF
CON room temperature → -78 deg C

STAGE(2)

RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 1 hour, -78 deg C
SUBSTAGE(2) -78 deg C → -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C → -78 deg C

STAGE(3)

RCT BI 75-77-4
CON 8 hours, -78 deg C → room temperature

STAGE(4)

RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO BJ 444109-28-8

RX(14) RCT BJ 444109-28-8

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BL 37342-97-5 Hydrozirconocene Cl
CON SUBSTAGE(1) 5 minutes, room temperature
SUBSTAGE(2) room temperature -> 55 deg C
SUBSTAGE(3) 1 hour, 55 deg C
SUBSTAGE(4) 55 deg C -> room temperature

STAGE(3)
RGT X 7553-56-2 I2
SOL 109-99-9 THF
CON 20 minutes, room temperature

PRO BK 444109-29-9

RX(15)

STAGE(1)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT BM 75-16-1
SOL 60-29-7 Et2O
CON 15 minutes, room temperature

STAGE(3)
RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC6H4)2
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂C₁₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 C1CH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3

SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)

SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)

RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)

RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)

RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)

SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)

SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)

CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

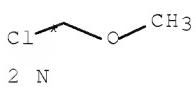
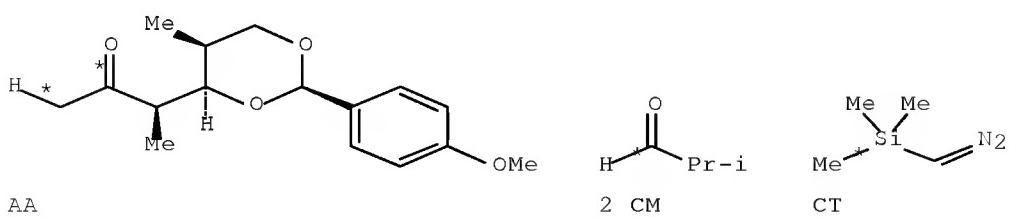
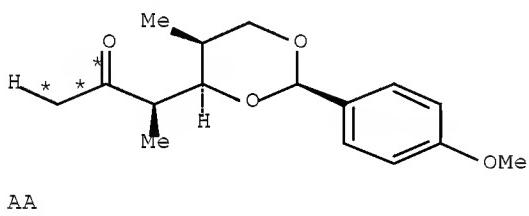
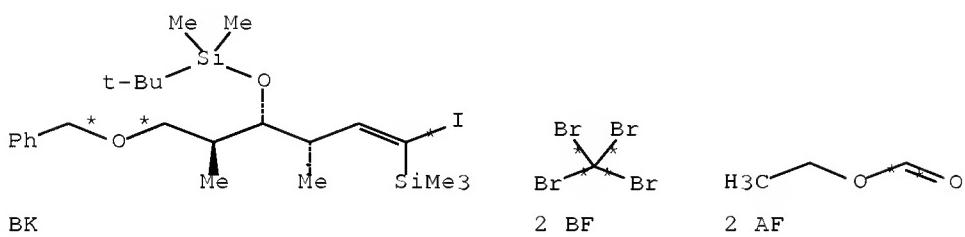
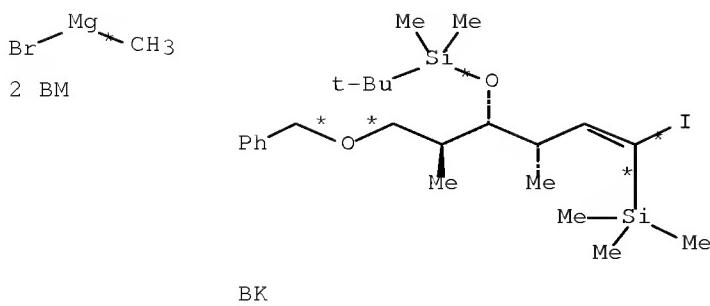
STAGE(3)

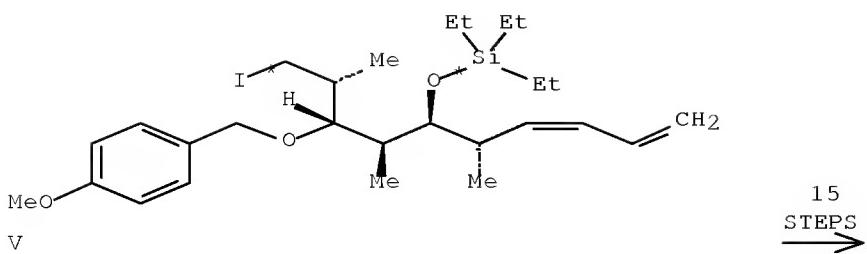
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

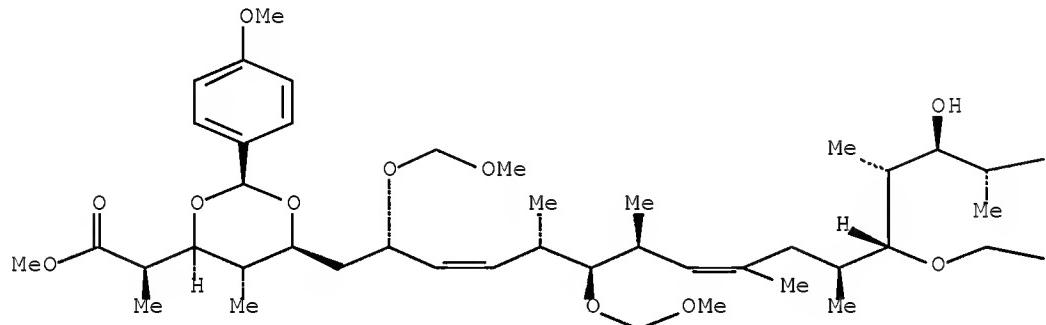
RX(529) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36)

RX(529) 2 BM + 2 BK + 2 BF + 2 AF + 2 AA + 2 CM + CT +
2 N + V ==> G





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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE (1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE (2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE (3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE (4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water

CON room temperature

PRO BN 444109-30-2
NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)
RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂C₁₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂C₁₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5

NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate
SOL 75-09-2 CH₂Cl₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH₂C₁₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H₂
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

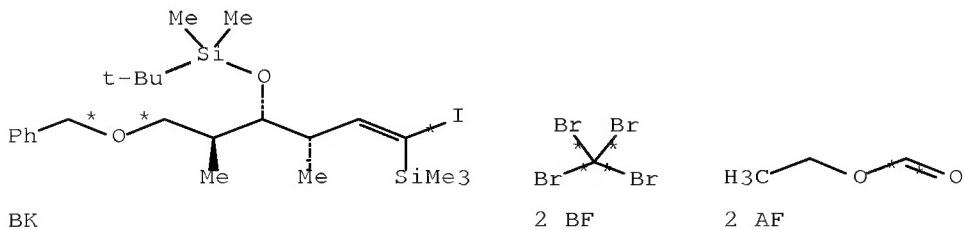
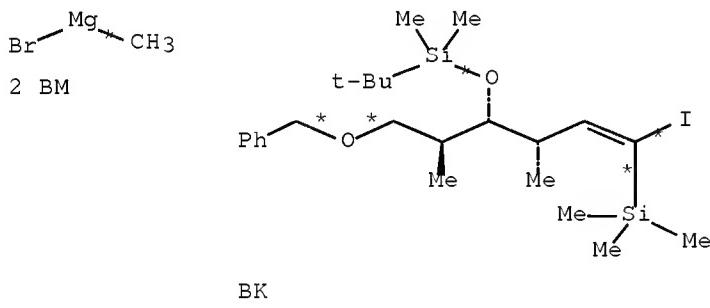
STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

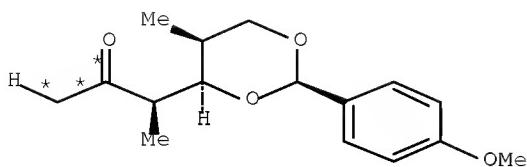
STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

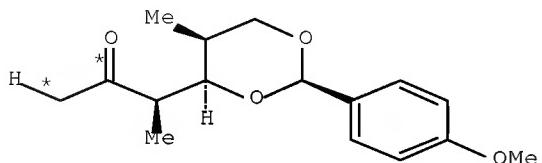
PRO G 851889-86-6
NTE last stage quench

RX(530) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36), RX(2)
RX(530) 2 BM + 2 BK + 2 BF + 2 AF + 2 AA + 2 CM + CT +
2 N + V + H ==> I

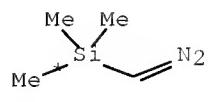
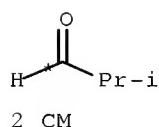




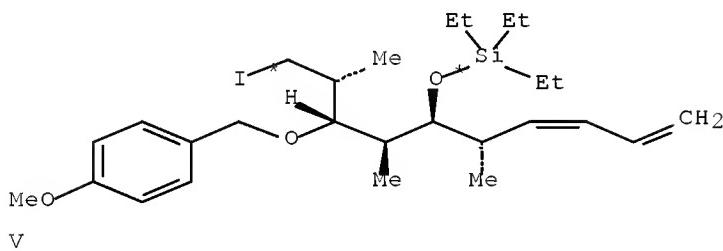
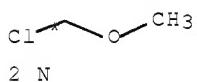
AA



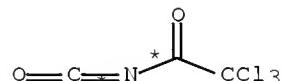
AA



CT

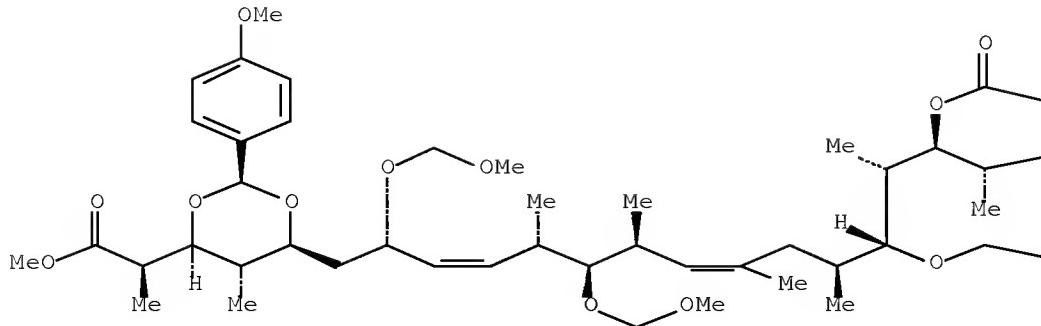


V



H

15
STEPS
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE(1)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RCT BM 75-16-1
SOL 60-29-7 Et₂O
CON 15 minutes, room temperature

STAGE(3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)
RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)2
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F3CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)

RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI₂
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe

SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)

RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)

RGT CW 7558-80-7 NaH2PO4, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)

SOL 60-29-7 Et2O
CON room temperature

STAGE(8)

RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)

SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)

RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7

NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)

RGT R 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)

RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)

SOL 110-54-3 Hexane

CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)

CAT 7440-05-3 Pd
CON room temperature

STAGE(4)

RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)

SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)

RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)

RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2

NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)

SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT P 64-19-7 AcOH, Q 429-41-4 Bu₄N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)

SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)

RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)

CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)

RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et₃N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH₂C₁₂

CON room temperature

STAGE (2)

RCT H 3019-71-4

CON 10 minutes, room temperature

STAGE (3)

SOL 67-56-1 MeOH

CON room temperature

STAGE (4)

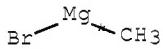
RGT J 584-08-7 K2CO3

CON 75 minutes, room temperature

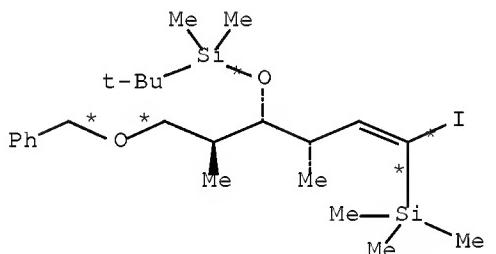
PRO I 851889-65-1

RX(567) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(32), RX(33), RX(34), RX(3), RX(35), RX(36), RX(2),
RX(37)

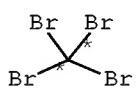
RX(567) BM + BK + BF + AF + AA + CM + CT + 2 N +
V + H ==> A



BM



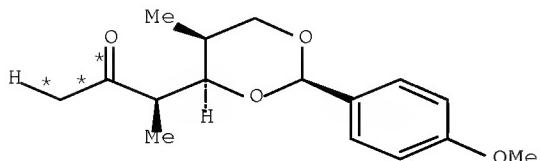
BK



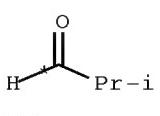
BF



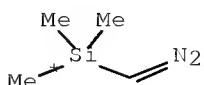
AF



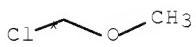
AA



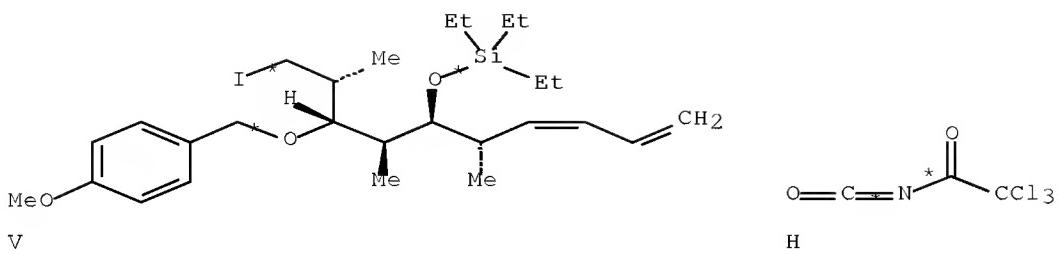
CM



CT

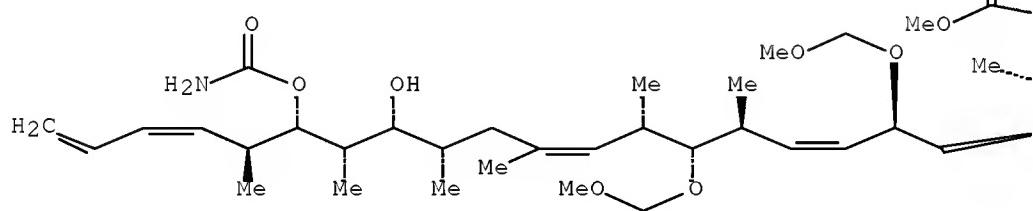


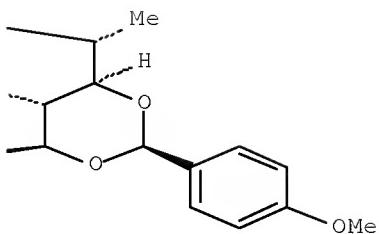
2 N



16
STEPS
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PAGE 1-A





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RX(15)

STAGE (1)

RGT BO 7646-85-7 ZnCl₂
 SOL 109-99-9 THF
 CON room temperature

STAGE (2)

RCT BM 75-16-1
 SOL 60-29-7 Et₂O
 CON 15 minutes, room temperature

STAGE (3)

RCT BK 444109-29-9
 CAT 14221-01-3 Pd(PPh₃)₄
 SOL 109-99-9 THF
 CON 2 hours, room temperature

STAGE (4)

RGT AI 12125-02-9 NH₄Cl
 SOL 7732-18-5 Water
 CON room temperature

PRO BN 444109-30-2
 NTE key step, stereoselective; last stage quench

RX(16)

STAGE (1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
 SOL 109-99-9 THF
 CON room temperature

STAGE (2)

RGT BT 7439-93-2 Li
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> 25 deg C
 SUBSTAGE(3) 5 hours, 15 - 25 deg C
 SUBSTAGE(4) 15 deg C -> room temperature

STAGE (3)

RCT BN 444109-30-2

SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3
NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)
RGT AQ 79-37-8 (COCl)2
SOL 75-09-2 CH2Cl2
CON room temperature -> -78 deg C

STAGE(2)
RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)
RCT BR 444109-31-3
SOL 75-09-2 CH2Cl2
CON 1 hour, -78 deg C

STAGE(4)
RGT AR 121-44-8 Et3N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7
NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)
RGT W 603-35-0 PPh3
SOL 75-09-2 CH2Cl2
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH2Cl2
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH4Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H₂O₂
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)

CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH₂CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na₂S₂O₃
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu₄N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO₃
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et₃N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH₂Cl₂
CON room temperature

STAGE(2)

RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

RX(37) RCT I 851889-65-1

STAGE(1)
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature

STAGE(2)
RGT D 144-55-8 NaHCO3
CON room temperature

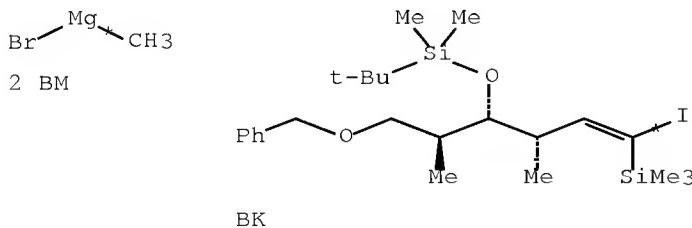
STAGE(3)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

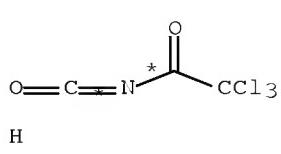
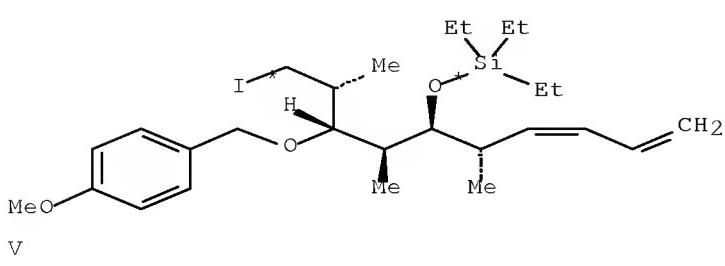
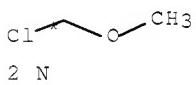
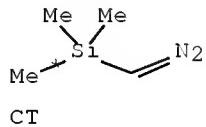
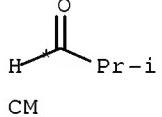
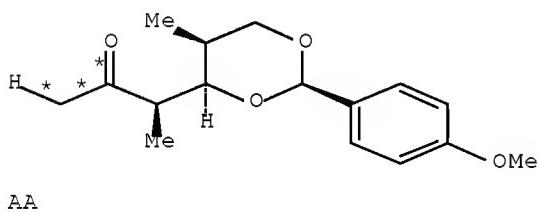
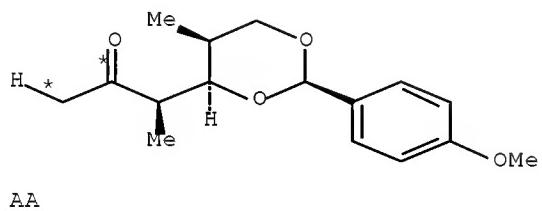
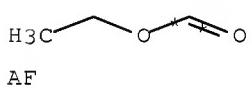
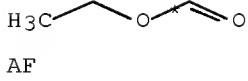
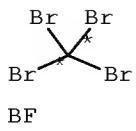
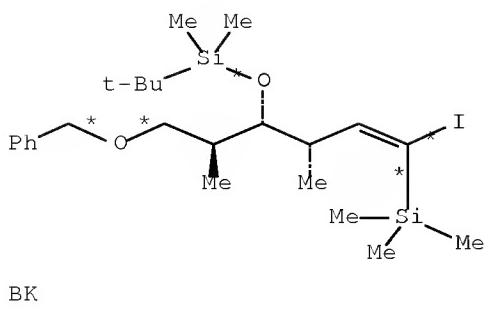
STAGE(4)
RGT DM 84-58-2 DDQ
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

PRO A 851889-87-7

RX(568) OF 576 COMPOSED OF RX(15), RX(16), RX(17), RX(18), RX(6), RX(28),
RX(29), RX(30), RX(31), RX(32), RX(33), RX(34), RX(3), RX(35),
RX(36), RX(2)

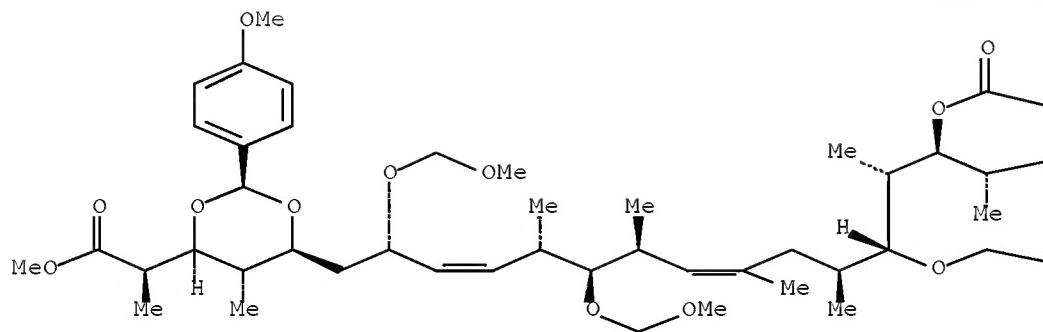
RX(568) 2 BM + 2 BK + BF + 2 AF + 2 AA + CM + CT + 2
N + V + H ==> I





16
STEPS
→

PAGE 1-A



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

RX(15)

STAGE (1)

RGT BO 7646-85-7 ZnCl₂
SOL 109-99-9 THF
CON room temperature

STAGE (2)

RCT BM 75-16-1
SOL 60-29-7 Et₂O
CON 15 minutes, room temperature

STAGE (3)

RCT BK 444109-29-9
CAT 14221-01-3 Pd(PPh₃)₄
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE (4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON room temperature

PRO BN 444109-30-2

NTE key step, stereoselective; last stage quench

RX(16)

STAGE(1)

RGT BS 1625-91-8 (p-t-BuC₆H₄)₂
SOL 109-99-9 THF
CON room temperature

STAGE(2)

RGT BT 7439-93-2 Li
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> 25 deg C
SUBSTAGE(3) 5 hours, 15 - 25 deg C
SUBSTAGE(4) 15 deg C -> room temperature

STAGE(3)

RCT BN 444109-30-2
SOL 109-99-9 THF
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) 2.5 hours, -78 deg C

STAGE(4)

RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON -78 deg C -> room temperature

PRO BR 444109-31-3

NTE first stage sonication; third stage inverse addn.; last stage quench

RX(17)

STAGE(1)

RGT AQ 79-37-8 (COCl)₂
SOL 75-09-2 CH₂Cl₂
CON room temperature -> -78 deg C

STAGE(2)

RGT AP 67-68-5 DMSO
CON 45 minutes, -78 deg C

STAGE(3)

RCT BR 444109-31-3
SOL 75-09-2 CH₂Cl₂
CON 1 hour, -78 deg C

STAGE(4)

RGT AR 121-44-8 Et₃N
CON SUBSTAGE(1) 15 minutes, -78 deg C
SUBSTAGE(2) 20 minutes, -78 deg C -> room temperature

PRO BU 444109-43-7

NTE last stage quench; Swern oxidn.

RX(18) RCT BF 558-13-4

STAGE(1)

RGT W 603-35-0 PPh₃
SOL 75-09-2 CH₂Cl₂
CON 10 minutes, 0 deg C

STAGE(2)
RCT BU 444109-43-7
RGT BH 108-48-5 2,6-Lutidine
SOL 75-09-2 CH₂C₁₂
CON 4 hours, 0 deg C

STAGE(3)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 0 deg C

PRO AE 444109-32-4
NTE last stage quench; Corey-Fuchs olefination

RX(6) RCT AE 444109-32-4

STAGE(1)
SOL 109-99-9 THF
CON room temperature -> -78 deg C

STAGE(2)
RGT AH 109-72-8 BuLi
SOL 110-54-3 Hexane
CON SUBSTAGE(1) 30 minutes, -78 deg C
SUBSTAGE(2) -78 deg C -> -20 deg C
SUBSTAGE(3) 1 hour, -20 deg C
SUBSTAGE(4) -20 deg C -> -78 deg C

STAGE(3)
RCT AF 109-94-4
CON SUBSTAGE(1) 2 hours, -78 deg C
SUBSTAGE(2) -78 deg C -> 30 deg C
SUBSTAGE(3) 8 hours, 30 deg C

STAGE(4)
RGT AI 12125-02-9 NH₄Cl
SOL 7732-18-5 Water
CON 30 deg C -> room temperature

PRO AG 444109-23-3
NTE last stage quench

RX(28) RCT AA 652986-45-3

STAGE(1)
SOL 75-09-2 CH₂C₁₂
CON room temperature -> -78 deg C

STAGE(2)
RGT R 7087-68-5 EtN(Pr-i)₂
CON 5 minutes, -78 deg C

STAGE(3)
RGT CK 60669-69-4 F₃CSO₃BBu₂
CON 45 minutes, -78 deg C

STAGE(4)
RCT AG 444109-23-3
SOL 75-09-2 CH₂C₁₂
CON 1 hour, -78 deg C

STAGE(5)
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) -78 deg C
SUBSTAGE(2) -78 deg C -> 0 deg C

STAGE(6)
RGT CL 7722-84-1 H2O2
SOL 7732-18-5 Water, 67-56-1 MeOH
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON room temperature

PRO CJ 851889-73-1
NTE key step, stereoselective (d.r. 30:1); fifth stage phosphate buffer; aldol reaction

RX(29) RCT CJ 851889-73-1

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RCT CM 78-84-2
CON room temperature -> -10 deg C

STAGE(3)
RGT CO 32248-43-4 SmI2
SOL 109-99-9 THF
CON 4 hours, -10 deg C

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water
CON -10 deg C -> room temperature

PRO CN 851889-75-3
NTE last stage quench

RX(30) RCT CN 851889-75-3

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature

STAGE(2)
RGT CR 1310-58-3 KOH
CON room temperature

PRO CP 851889-76-4, CQ 851889-77-5
NTE reaction monitored by TLC

RX(31) RCT CQ 851889-77-5
PRO CP 851889-76-4
CAT 24057-28-1 Pyridinium tosylate

SOL 75-09-2 CH₂C₁₂
NTE no reaction details

RX(32) RCT CP 851889-76-4

STAGE(1)
SOL 71-43-2 Benzene
CON room temperature

STAGE(2)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 2 hours, room temperature

STAGE(3)
CAT 15529-49-4 RuCl₂(PPh₃)₃
CON 6 hours, room temperature

STAGE(4)
RGT CV 513-35-9 Me₂C:CHMe
SOL 75-65-0 t-BuOH
CON room temperature

STAGE(5)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(6)
RGT CW 7558-80-7 NaH₂PO₄, CX 7758-19-2 NaOClO
SOL 7732-18-5 Water
CON 1 hour, room temperature

STAGE(7)
SOL 60-29-7 Et₂O
CON room temperature

STAGE(8)
RGT C 7647-01-0 HCl
SOL 7732-18-5 Water
CON room temperature

STAGE(9)
SOL 67-56-1 MeOH, 71-43-2 Benzene
CON room temperature

STAGE(10)
RCT CT 18107-18-1
SOL 110-54-3 Hexane
CON 15 minutes, room temperature

PRO CU 851889-79-7
NTE last stage acidification

RX(33) RCT CU 851889-79-7

STAGE(1)
RGT R 7087-68-5 EtN(Pr-i)₂
SOL 75-09-2 CH₂C₁₂
CON room temperature -> 0 deg C

STAGE(2)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(3)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(4)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO DB 851889-80-0

RX(34) RCT DB 851889-80-0

STAGE(1)
SOL 110-54-3 Hexane
CON room temperature

STAGE(2)
CAT 91-22-5 Quinoline
CON room temperature

STAGE(3)
CAT 7440-05-3 Pd
CON room temperature

STAGE(4)
RGT DC 1333-74-0 H2
CON 8 hours, room temperature

STAGE(5)
SOL 107-14-2 ClCH2CN, 75-05-8 MeCN
CON room temperature

STAGE(6)
RGT DD 516-12-1 Iodosuccinimide
CON 3 hours, room temperature

STAGE(7)
RGT DE 7772-98-7 Na2S2O3
SOL 7732-18-5 Water
CON room temperature

PRO M 851889-82-2
NTE stereoselective; third stage Lindlar catalyst; sixth stage in dark; last stage quench

RX(3) RCT M 851889-82-2

STAGE(1)
SOL 109-99-9 THF
CON room temperature

STAGE(2)
RGT P 64-19-7 AcOH, Q 429-41-4 Bu4N.F
SOL 109-99-9 THF
CON 36 hours, room temperature

STAGE(3)
SOL 7732-18-5 Water
CON room temperature, pH 7

STAGE(4)
RGT R 7087-68-5 EtN(Pr-i)2
SOL 56-23-5 CC14
CON room temperature -> 0 deg C

STAGE(5)
CAT 1122-58-3 4-DMAP
CON 0 deg C

STAGE(6)
RCT N 107-30-2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 8 hours, 0 deg C -> room temperature

STAGE(7)
RGT D 144-55-8 NaHCO3
SOL 7732-18-5 Water

PRO O 851889-66-2
NTE third stage quench

RX(35) RCT V 216669-69-1

STAGE(1)
SOL 60-29-7 Et2O
CON room temperature -> -78 deg C

STAGE(2)
RGT DK 594-19-4 t-BuLi
SOL 109-66-0 Pentane
CON 30 minutes, -78 deg C

STAGE(3)
RGT BO 7646-85-7 ZnCl2
SOL 109-99-9 THF
CON SUBSTAGE(1) 5 minutes, -78 deg C
SUBSTAGE(2) 30 minutes, -78 deg C -> 0 deg C

STAGE(4)
RCT O 851889-66-2
CAT 14221-01-3 Pd(PPh3)4
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 6 hours, room temperature

STAGE(5)
SOL 7732-18-5 Water
CON room temperature

PRO DJ 851889-85-5
NTE last stage quench

RX(36) RCT DJ 851889-85-5

STAGE(1)
SOL 67-56-1 MeOH
CON room temperature -> 0 deg C

STAGE(2)
CAT 104-15-4 TsOH
CON 1 hour, 0 deg C

STAGE(3)
RGT AR 121-44-8 Et3N
CON 0 deg C

PRO G 851889-86-6
NTE last stage quench

RX(2) RCT G 851889-86-6

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature

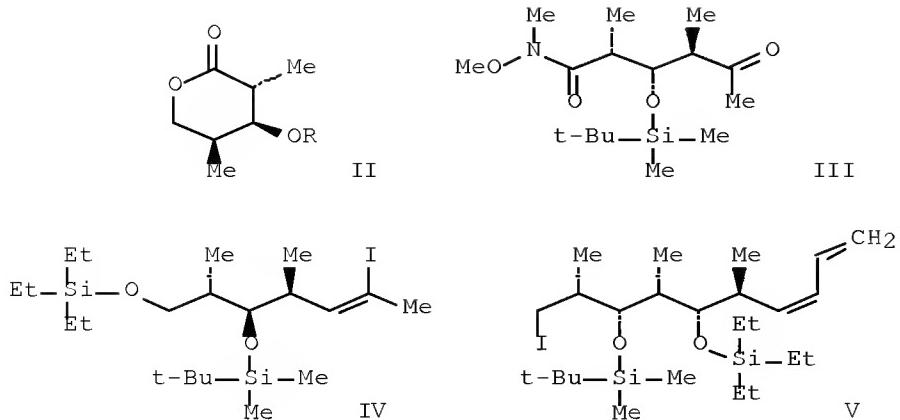
STAGE(2)
RCT H 3019-71-4
CON 10 minutes, room temperature

STAGE(3)
SOL 67-56-1 MeOH
CON room temperature

STAGE(4)
RGT J 584-08-7 K2CO3
CON 75 minutes, room temperature

PRO I 851889-65-1

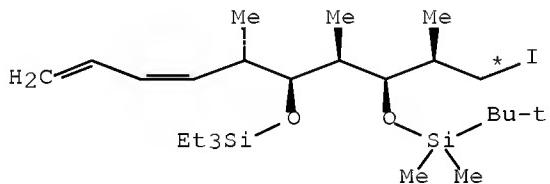
L3 ANSWER 7 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:447055 CASREACT Full-text
TITLE: A Formal Synthesis of (+)-Discodermolide
AUTHOR(S): Loiseleur, Olivier; Koch, Guido; Cercus, Jacques;
Schuerch, Friedrich
CORPORATE SOURCE: Chemical and Analytical Development, Novartis Pharma
AG, Basel, CH-4002, Switz.
SOURCE: Organic Process Research & Development (2005), 9(3),
259-271
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



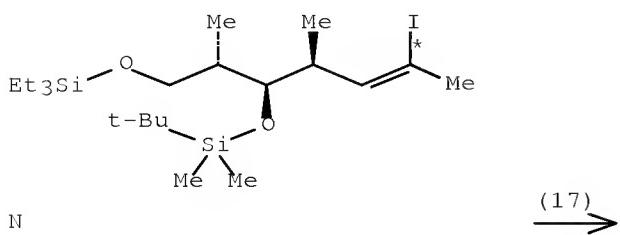
AB Herein, we report the formal synthesis of (+)-discodermolide (I), a promising anticancer agent of sponge origin, in 24 linear steps, with 35 steps in total. The route proceeds from lactone II ($R = SiMe_2CMe_3, SiEt_3$), a building block containing the common 1,2-anti-2,3-syn stereotriad found in each of the three subunits, Me ketone III (C1-C6), vinyl iodide IV (C9-C14), and iodide V (C15-C24) utilized for the construction of I. The key fragment union was achieved by a Suzuki cross-coupling between IV and V.

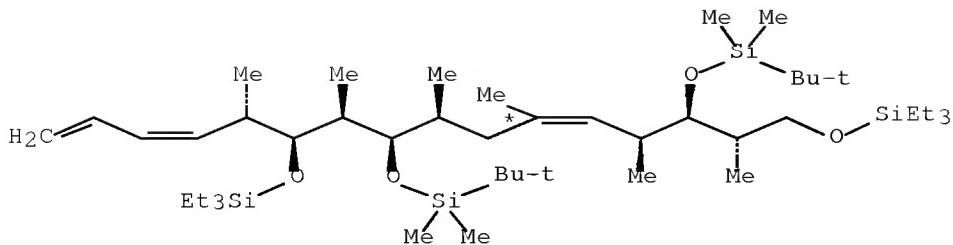
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(17) OF 86 ...R + N ==> BE...



R





BE
YIELD 81%

RX(17) RCT R 649755-91-9

STAGE(1)

RGT BF 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane
 CON 5 minutes, -80 - -75 deg C

STAGE(2)

RGT BG 38050-71-4 9-BBN-OMe
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -80 - -75 deg C
 SUBSTAGE(2) 90 minutes, -80 - -75 deg C -> 23 deg C

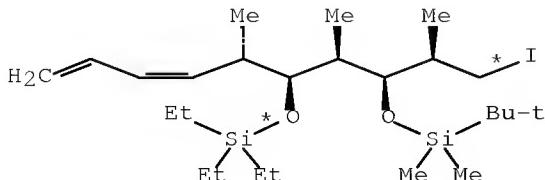
STAGE(3)

RCT N 851316-82-0
 RGT BH 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON SUBSTAGE(1) 30 minutes, 23 deg C
 SUBSTAGE(2) 30 minutes, 23 deg C

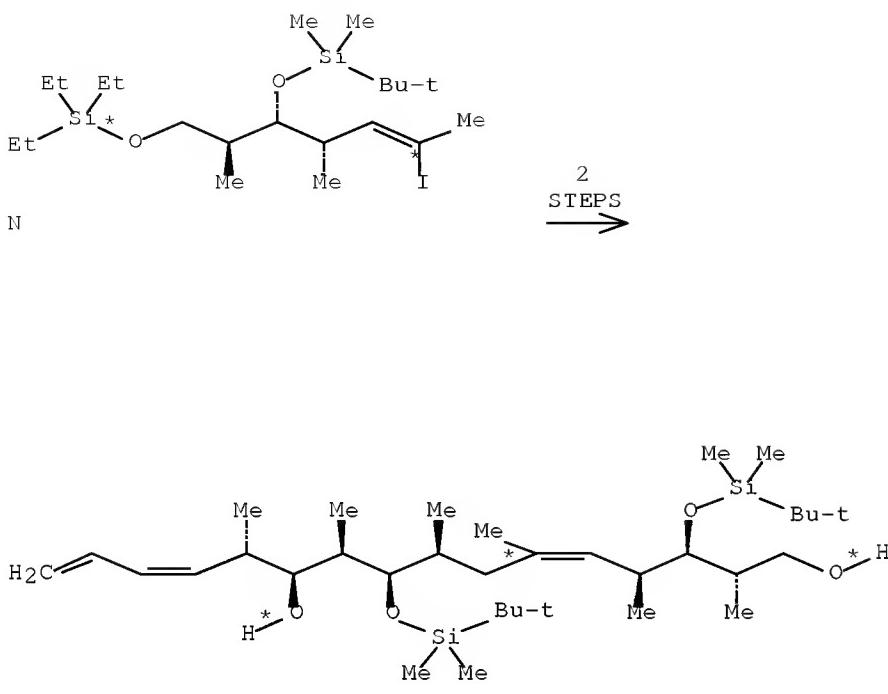
PRO BE 649755-93-1

NTE stereoselective

RX(33) OF 86 COMPOSED OF RX(17), RX(18)
 RX(33) R + N ==> BJ



R



BJ
YIELD 77%

RX(17) RCT R 649755-91-9

STAGE(1)

RGT BF 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane
 CON 5 minutes, -80 - -75 deg C

STAGE(2)

RGT BG 38050-71-4 9-BBN-OMe
 SOL 109-99-9 THF
 CON SUBSTAGE(1) 5 minutes, -80 - -75 deg C
 SUBSTAGE(2) 90 minutes, -80 - -75 deg C -> 23 deg C

STAGE(3)

RCT N 851316-82-0
 RGT BH 534-17-8 Cs2CO3
 CAT 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON SUBSTAGE(1) 30 minutes, 23 deg C
 SUBSTAGE(2) 30 minutes, 23 deg C

PRO BE 649755-93-1

NTE stereoselective

RX(18) RCT BE 649755-93-1
 RGT BK 76-05-1 F3CCO2H

PRO BJ 261968-23-4
 SOL 7732-18-5 Water, 109-99-9 THF
 CON SUBSTAGE(1) 23 deg C
 SUBSTAGE(2) 17 hours, 23 deg C
 NTE chemoselective

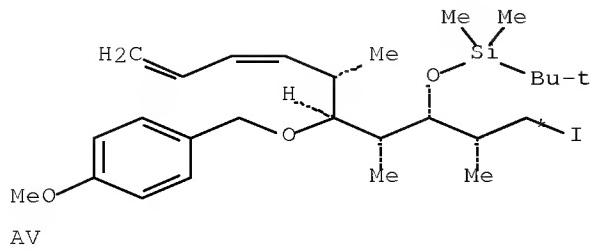
L3 ANSWER 8 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 142:411149 CASREACT Full-text
 TITLE: Synthesis of discodermolide and variants thereof
 INVENTOR(S): Smith, Amos B., III; Freeze, Brian Scott; Xian, Ming
 PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
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 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
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WO 2005035489	A3	20050804		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20070276144	A1	20071129	US 2007-575136	20070509
PRIORITY APPLN. INFO.:			US 2003-510097P	20031009
			WO 2004-US33473	20041012
OTHER SOURCE(S):	MARPAT 142:411149			
GI				

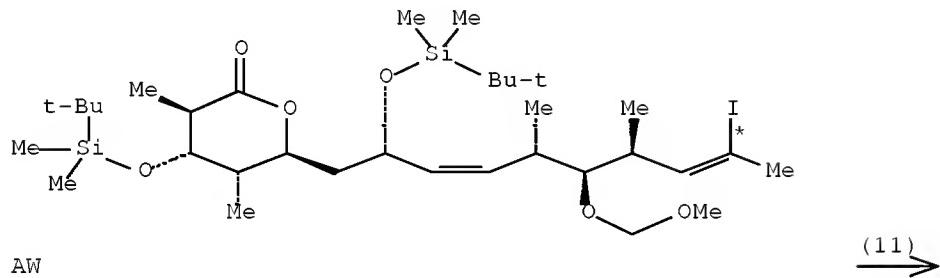
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Processes for synthesizing discodermolide and variants thereof such as I [R0 = alkyl, alkenyl, alkynyl, (CH₂)_ncycloalkyl, (CH₂)_naryl, (CH₂)_nheterocycle, wherein n = 0-4; R1, R2, R3, R6, R7, R8, R11, R12 = H, alkyl; R4, R9, R14, R15 = H, an acid labile hydroxyl protecting group; R10 = H, alkyl; R25 = H, an oxidation labile hydroxyl protecting group; Y = O, H₂I], are provided by reacting II with III [X1, X2 = halo, triflate, tosylate, mesylate]. Thus, intermediate I [R0 = CH:CH₂; R1, R2, R3, R6, R7, R8, R11, R12 = Me; R4, R14, R15 = TBS; R9 = MOM; R25 = PMB; Y = O (IV)], was prepared via a multistep synthetic sequence starting from methyl-(2S)-3-hydroxy-2-methyl-propionate. The synthetic utility of IV was subsequently demonstrated by its use in the preparation of (+)-discodermolide.

RX(11) OF 354 ...AV + AW ==> AX...

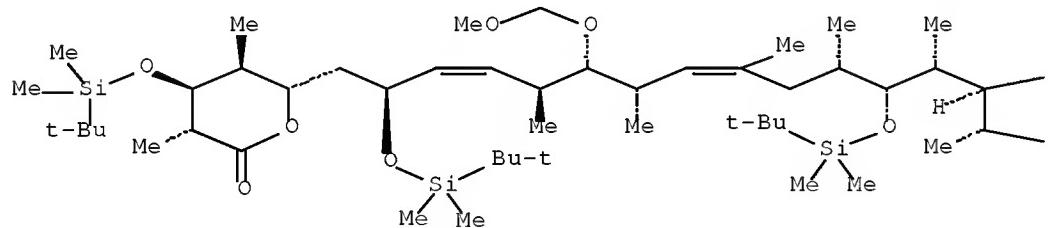


AV

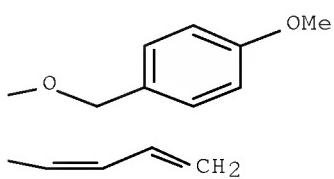


AW

PAGE 1-A



PAGE 1-B



AX
YIELD 50%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

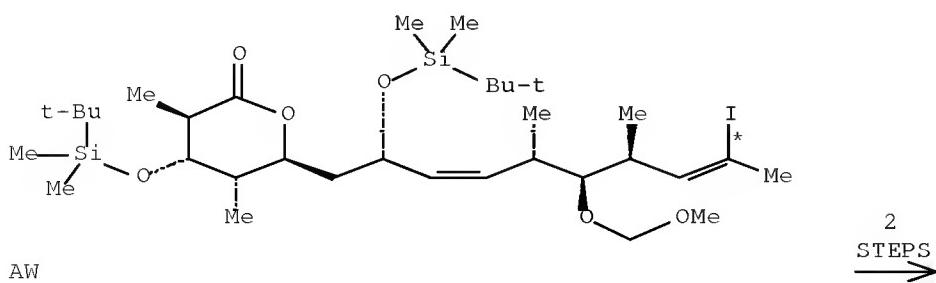
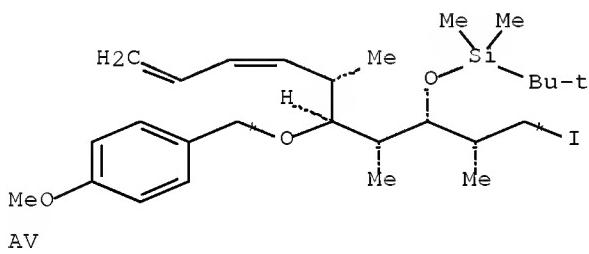
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

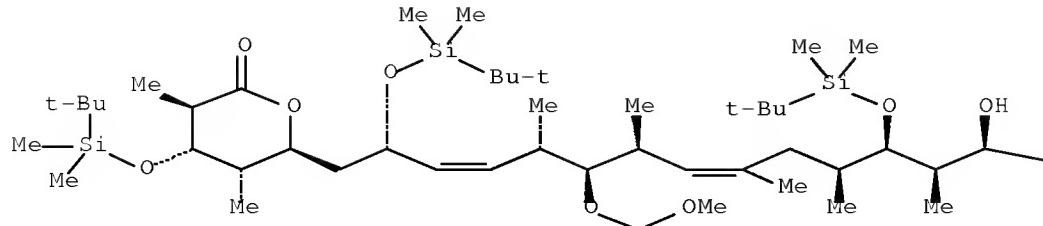
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(44) OF 354 COMPOSED OF RX(11), RX(28)

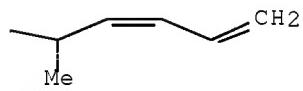
RX(44) AV + AW ==> CO



PAGE 1-A



PAGE 1-B



CO
YIELD 91%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

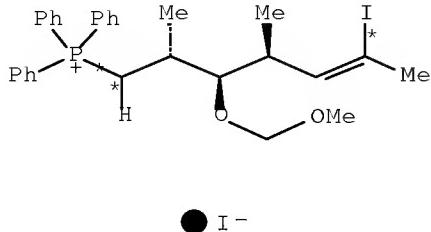
RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

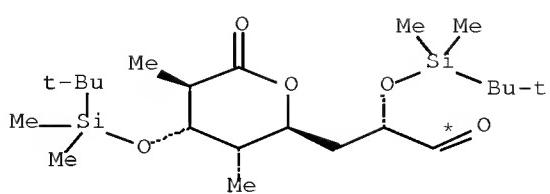
SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

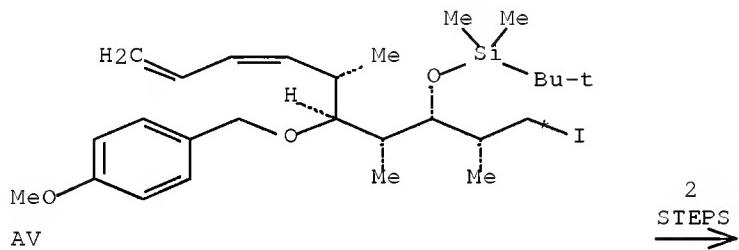
RX(61) OF 354 COMPOSED OF RX(27), RX(11)
RX(61) CE + CN + AV ==> AX



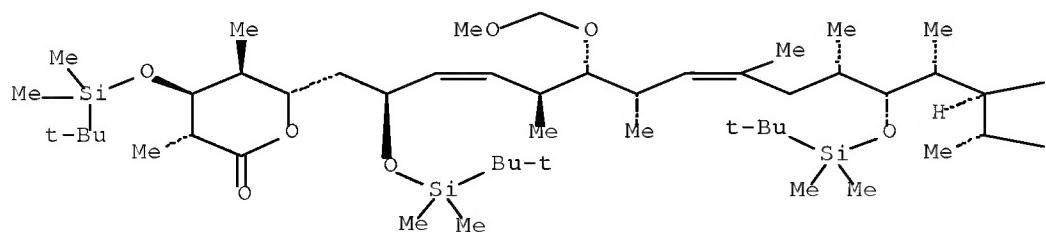
CE

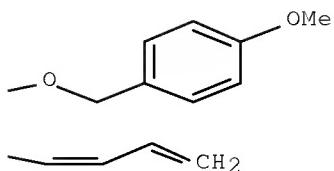


CN



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AX
YIELD 50%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

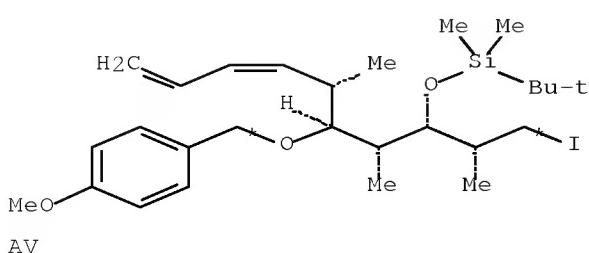
STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

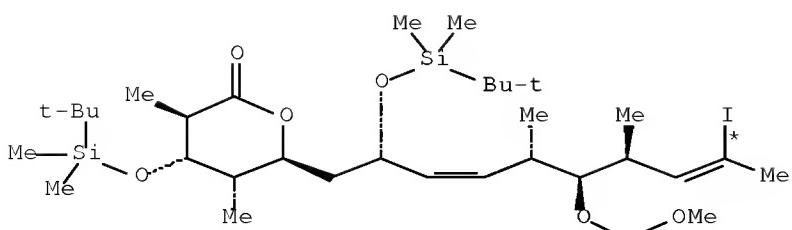
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

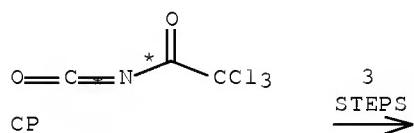
RX(87) OF 354 COMPOSED OF RX(11), RX(28), RX(29)
 RX(87) AV + AW + CP ==> CO



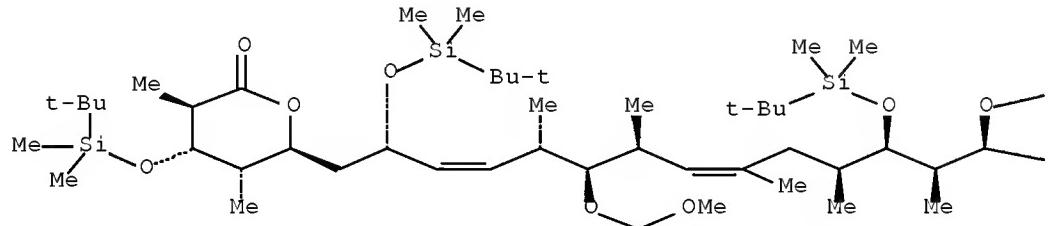
AV



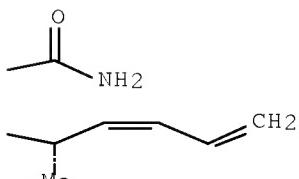
AW



PAGE 1-A



PAGE 1-B



CO
 YIELD 92%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

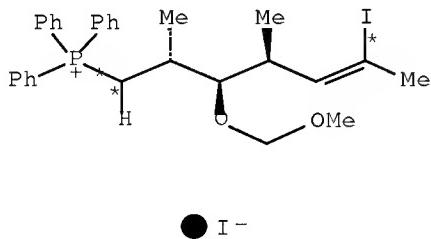
RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

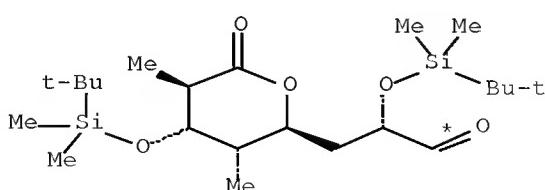
PRO CQ 633293-93--3

RX(89) OF 354 COMPOSED OF RX(27), RX(11), RX(28), RX(29)

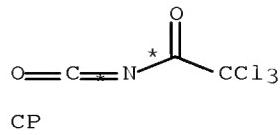
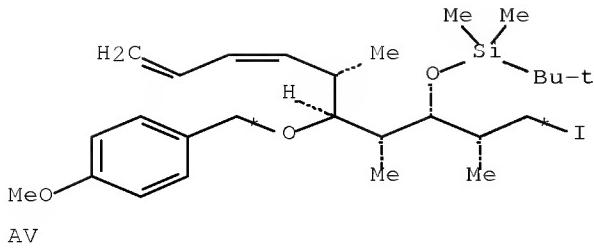
RX(89) CE + CN + AV + CP ==> CQ



CE

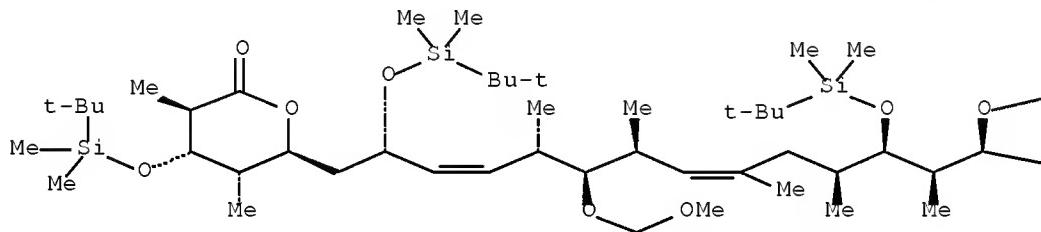


CN

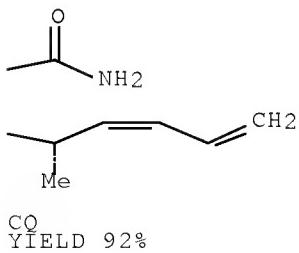


4
STEPS
→

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PAGE 1-B



RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 $(\text{Me}_3\text{Si})_2\text{N} \cdot \text{Na}$
 PRO AW 850211-74-4
 CON -78 deg C → -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

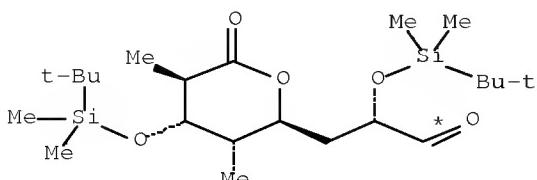
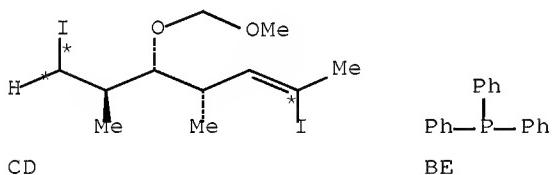
RX(29) RCT CO 633293-76-2, CP 3019-71-4

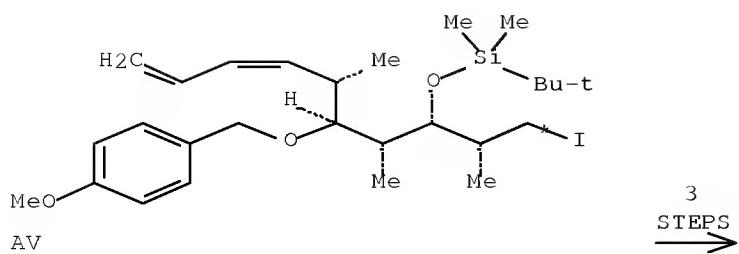
RGT CR 1344-28-1 Al2O3

PRO CQ 633293-93--3

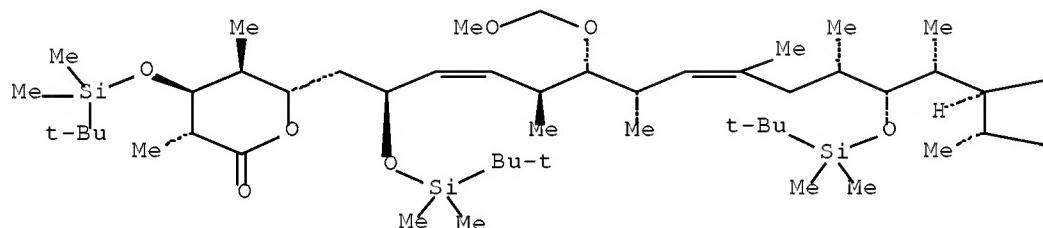
RX(115) OF 354 COMPOSED OF RX(23), RX(27), RX(11)

RX(115) CD + BE + CN + AV ==> AX

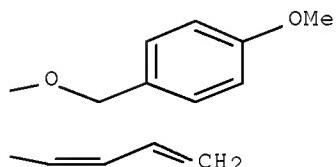




PAGE 1-A



PAGE 1-B



AX
YIELD 50%

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C → -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

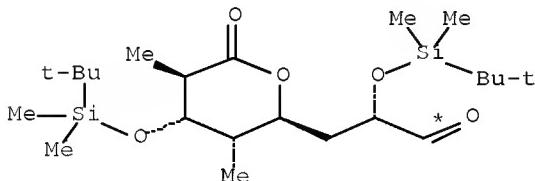
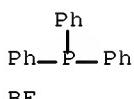
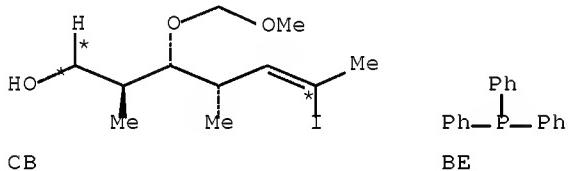
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

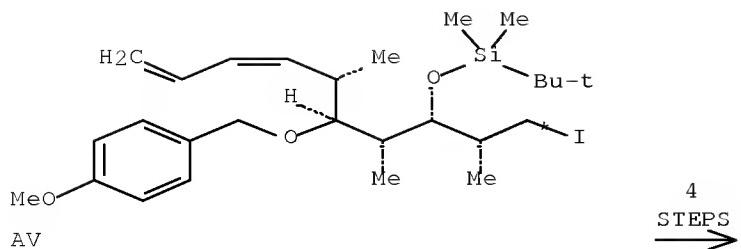
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

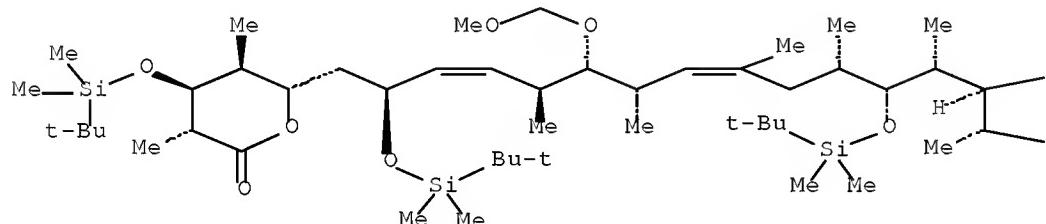
RX(116) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11)

RX(116) CB + BE + CN + AV ==> AX

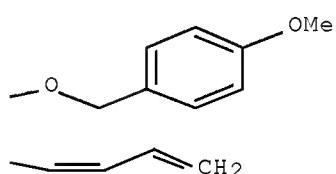




PAGE 1-A



PAGE 1-B



^{AX}
YIELD 50%

- RX(22) RCT CB 850211-70-0
 RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
 PRO CD 850211-71-1
- RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%
- RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C → -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
- RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

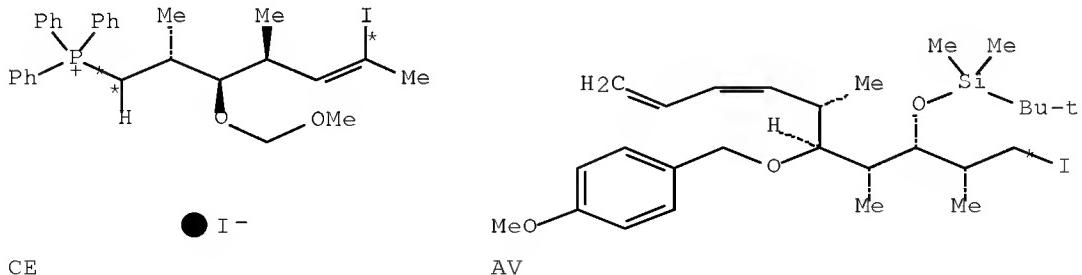
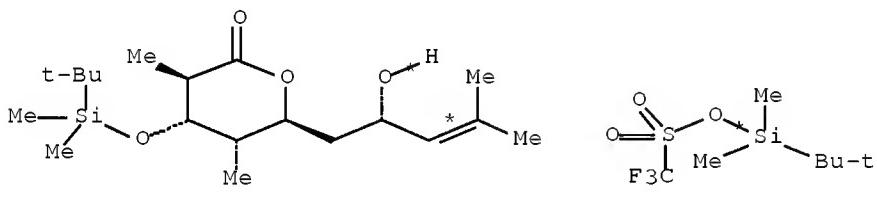
STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

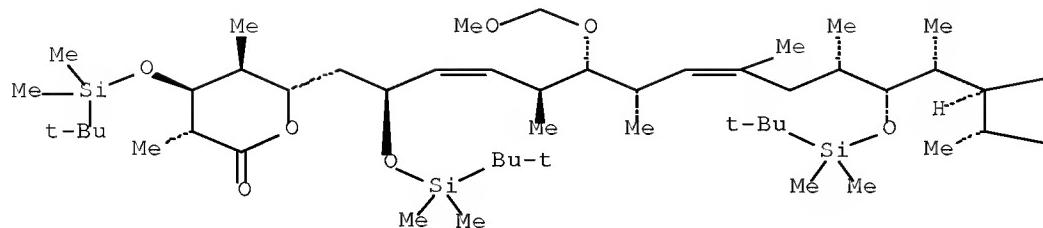
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(121) OF 354 COMPOSED OF RX(26), RX(27), RX(11)
 RX(121) CM + L + CE + AV ==> AX

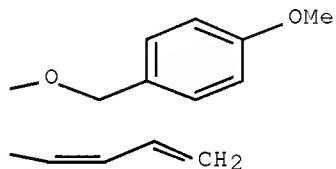


3
STEPS
→

PAGE 1-A



PAGE 1-B



^{AX}
YIELD 50%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂Cl₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C → -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

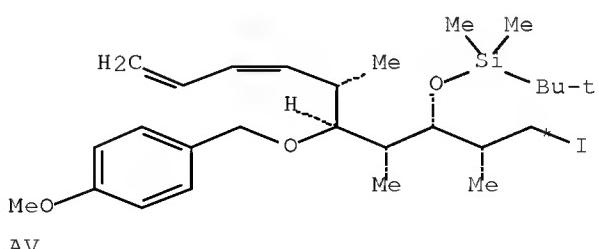
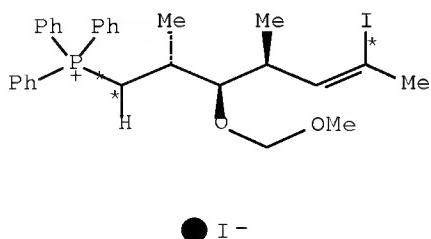
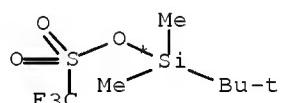
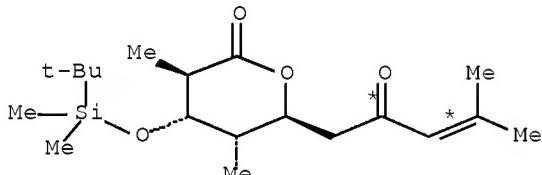
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

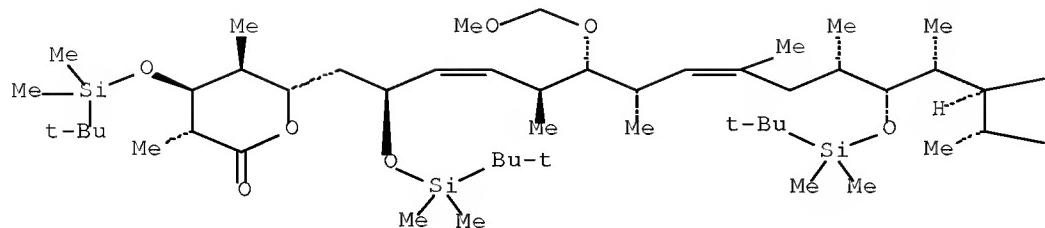
RX(122) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11)

RX(122) CJ + L + CE + AV ==> AX

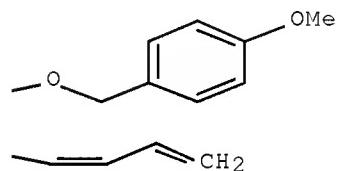


4
STEPS
→

PAGE 1-A



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^{AX}
YIELD 50%

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE (1)
SOL 75-09-2 CH₂Cl₂

STAGE (2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE (3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C → -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature → -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C → room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

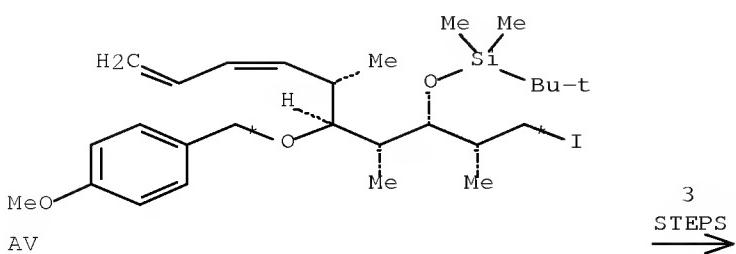
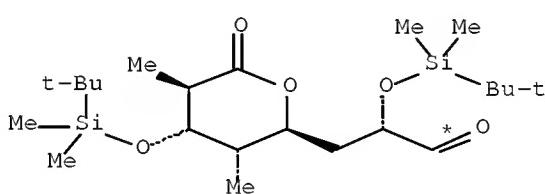
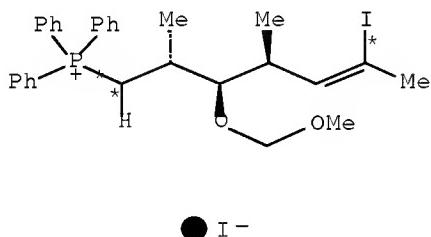
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

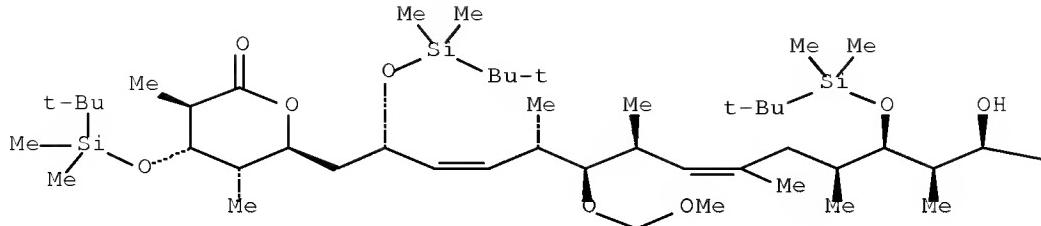
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(123) OF 354 COMPOSED OF RX(27), RX(11), RX(28)

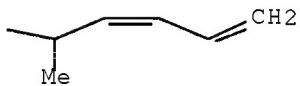
RX(123) CE + CN + AV ==> CO



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PAGE 1-B



CO
YIELD 91%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

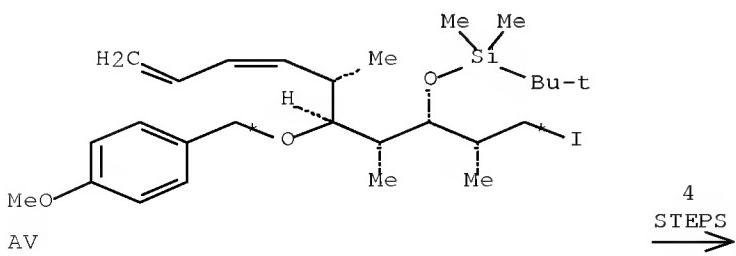
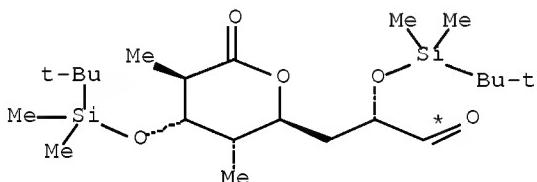
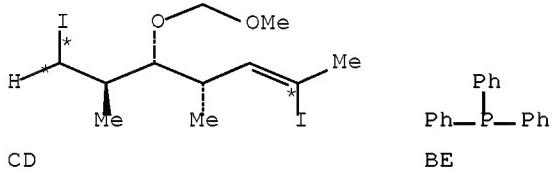
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

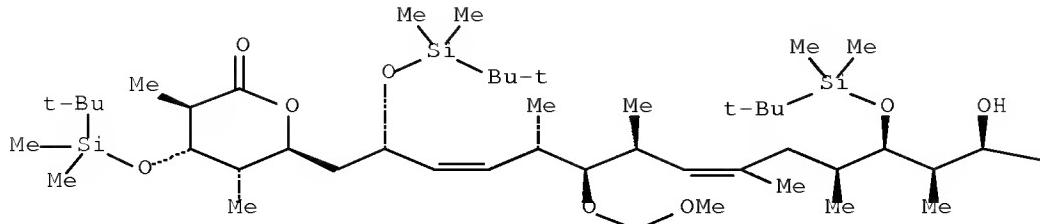
CON 0 - room temperature deg C

RX(124) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28)

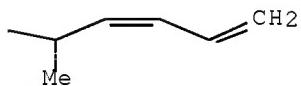
RX(124) CD + BE + CN + AV ==> CO



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CO
YIELD 91%

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDO

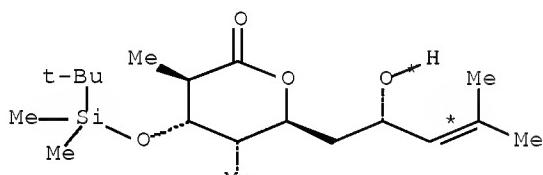
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂

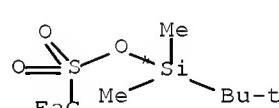
CON 0 = room temperature deg C

RX(125) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28)

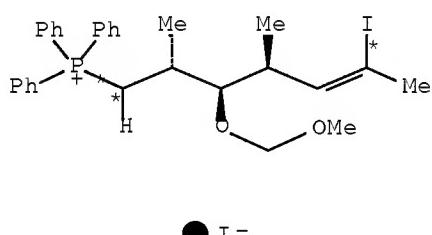
$$BX(125) \quad CM \pm L \pm CE \pm AV \implies CO$$



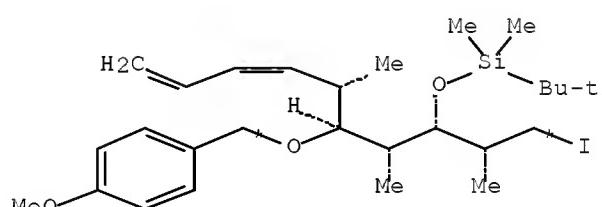
CM



L



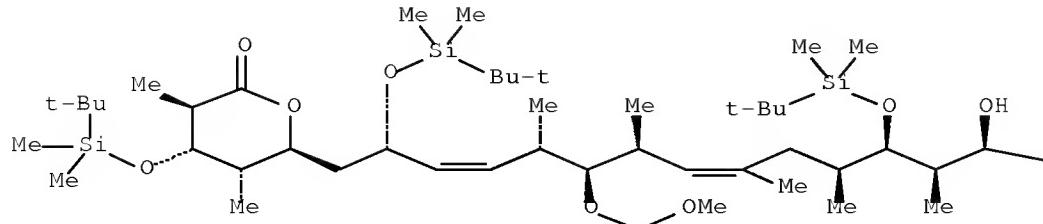
CE



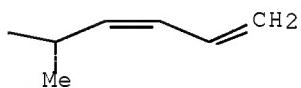
AV

4
STEPS
→

PAGE 1-A



PAGE 1-B



CO
YIELD 91%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C → -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature → -78 deg C
SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

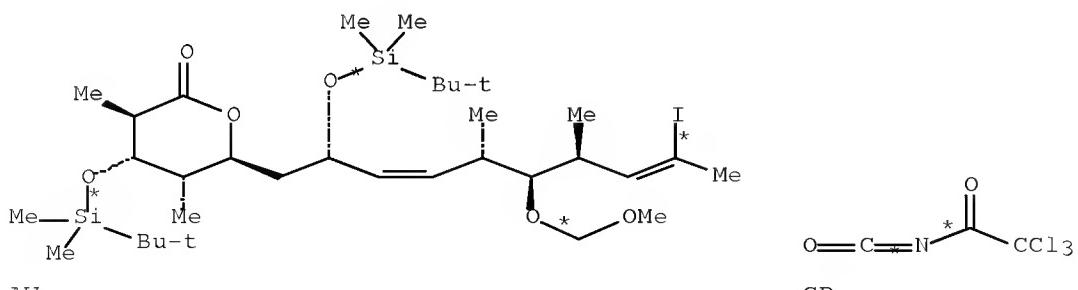
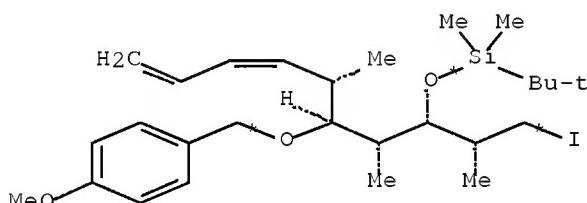
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

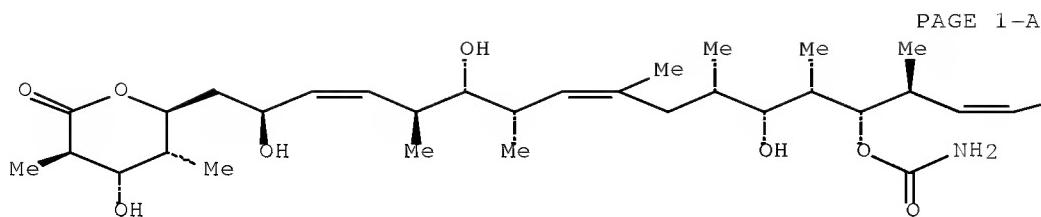
CON 0 - room temperature deg C

RX(127) OF 354 COMPOSED OF RX(11), RX(28), RX(29), RX(30)

RX(127) AV + AW + CP ==> CS



4
STEPS
→



PAGE 1-B



CS
YIELD 95%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature → -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

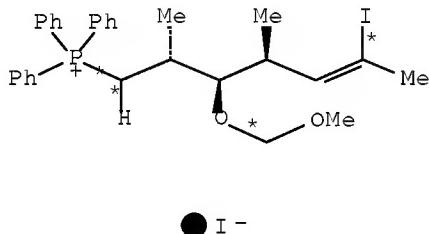
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

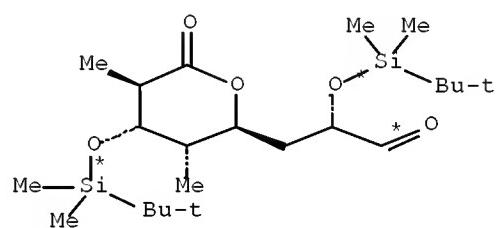
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al₂O₃
PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

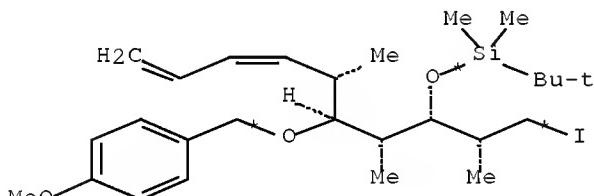
RX(175) OF 354 COMPOSED OF RX(27), RX(11), RX(28), RX(29), RX(30)
RX(175) CE + CN + AV + CP ==> CS



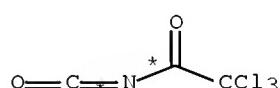
CE



CN

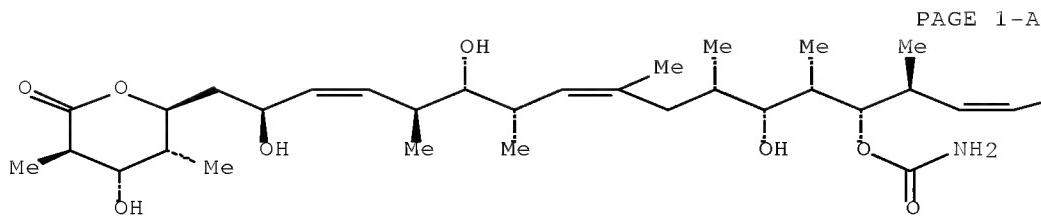


AV



CP

5
STEPS
→



PAGE 1-B



^{CS}
YIELD 95%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

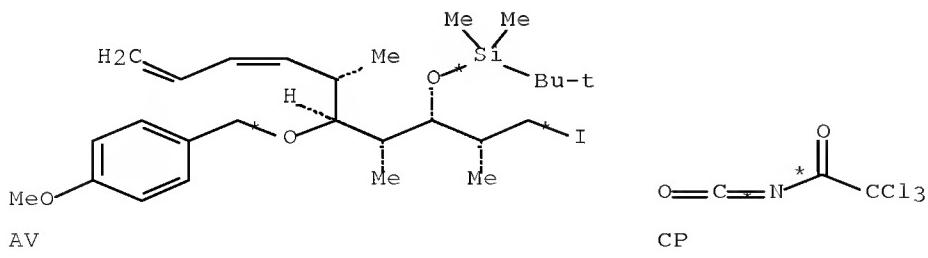
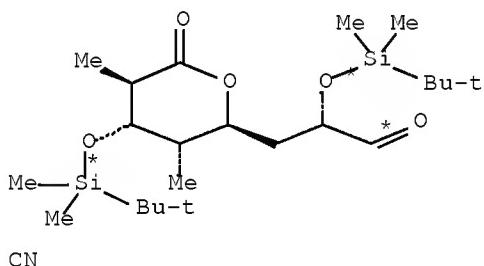
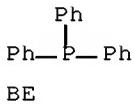
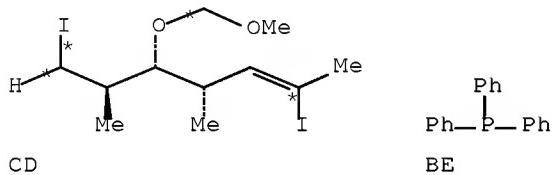
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

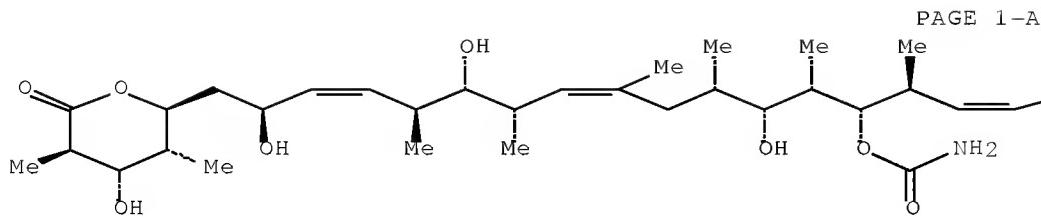
RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(178) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28), RX(29), RX(30)
RX(178) CD + BE + CN + AV + CP ==> CS



6
STEPS
→



PAGE 1-B

$\text{CH}_2=\text{CH}_2$
CS
YIELD 95%

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C → -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature → -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

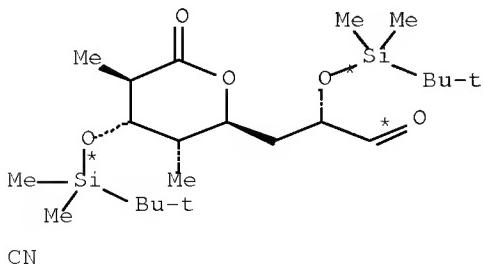
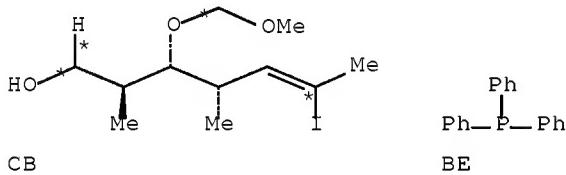
PRO CS 127943-53-7

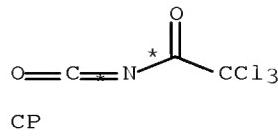
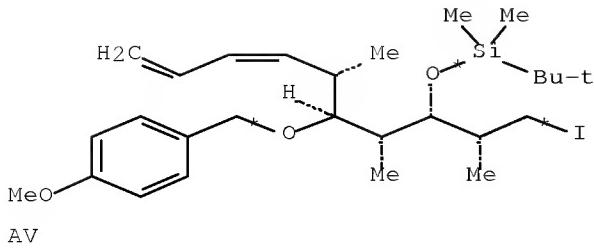
SOL 7732-18-5 Water, 67-56-1 MeOH

NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

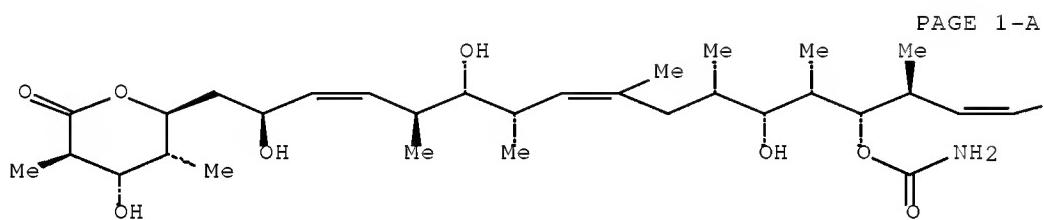
RX(179) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28), RX(29),
RX(30)

RX(179) CB + BE + CN + AV + CP ==> CS

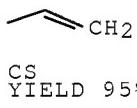




7
STEPS
→



PAGE 1-B



- RX(22) RCT CB 850211-70-0
RGT BE 603-35-0 PPh₃, BF 7553-56-2 I₂, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1
- RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%
- RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C → -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

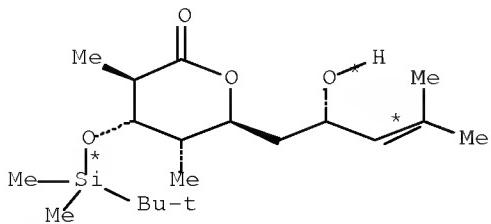
PRO CS 127943-53-7

SOL 7732-18-5 Water, 67-56-1 MeOH

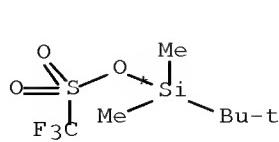
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(180) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

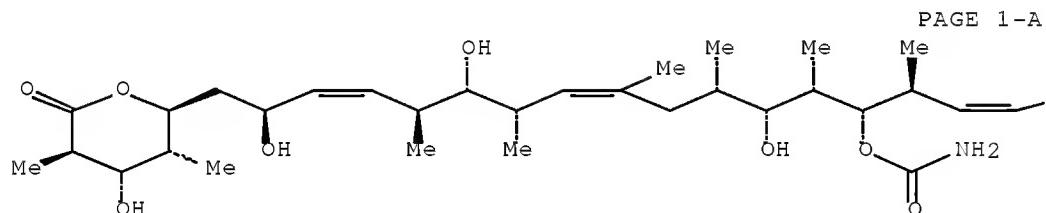
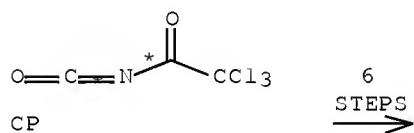
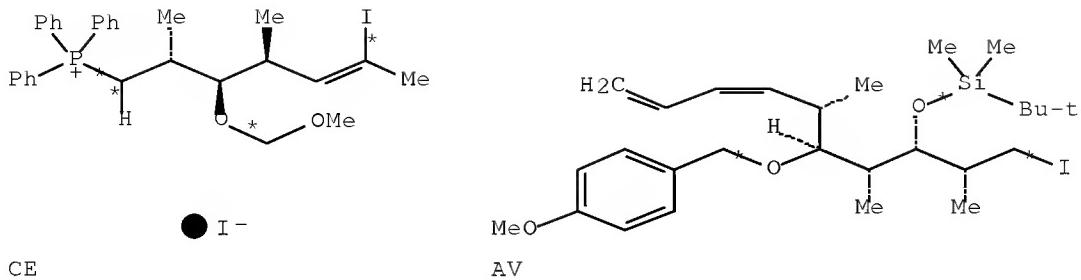
RX(180) CM + L + CE + AV + CP ==> CS



CM



L



PAGE 1-B



CS
YIELD 95%

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al₂O₃

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

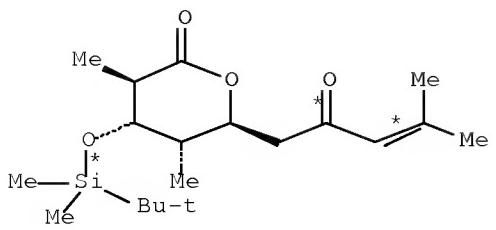
PRO CS 127943-53-7

SOL 7732-18-5 Water, 67-56-1 MeOH

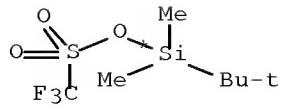
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(181) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28), RX(29),
RX(30)

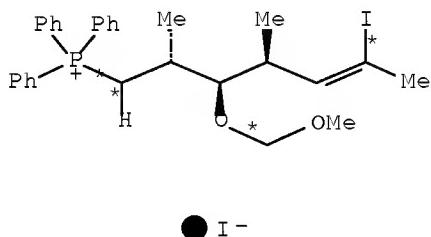
RX(181) CJ + L + CE + AV + CP ==> CS



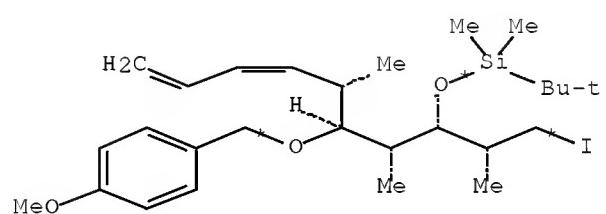
CJ



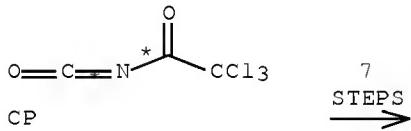
L



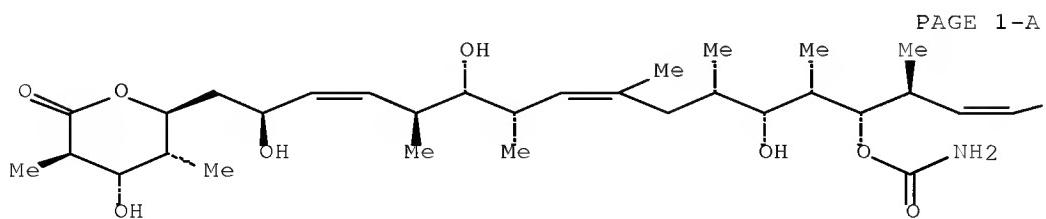
CE



AV



7
STEPS





CS
YIELD 95%

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH₂Cl₂

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH₂Cl₂

STAGE(3)
 RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

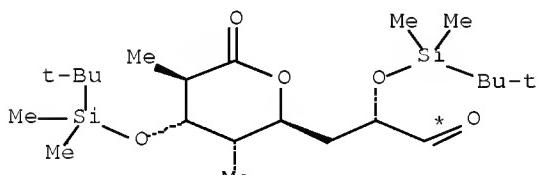
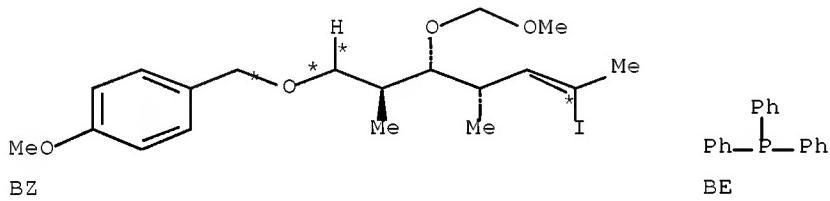
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

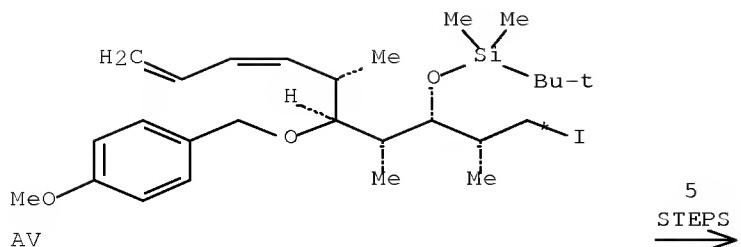
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al₂O₃
PRO CQ 633293-93-3

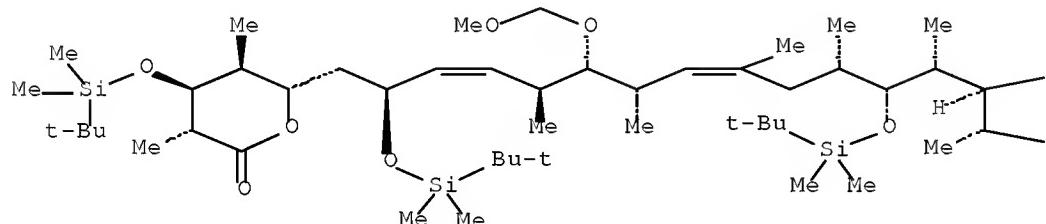
RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(222) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11)
RX(222) BZ + BE + CN + AV ==> AX

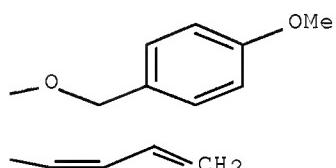




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AX
YIELD 50%

RX(21)	RCT	BZ	633294-02-7
	RGT	CC	84-58-2 DDQ
	PRO	CB	850211-70-0
	SOL		7732-18-5 Water

RX(22) RCT CB 850211-70-0
RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
 RX(11) RCT AV 850211-69-7

STAGE(1)

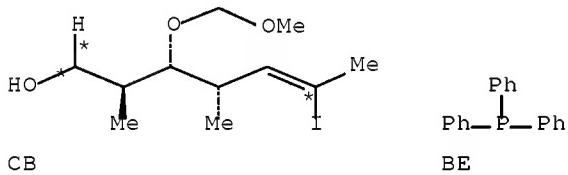
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

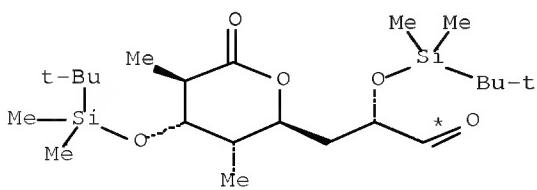
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

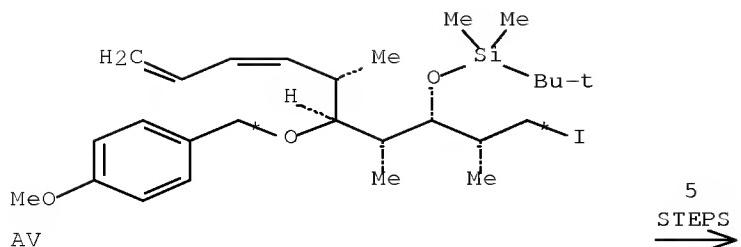
RX(226) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28)
 RX(226) CB + BE + CN + AV ==> CO



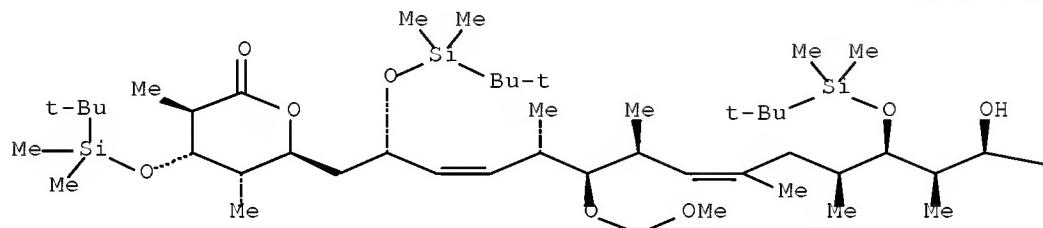
CB BE



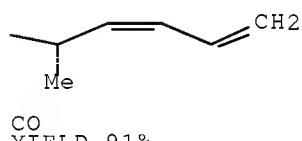
CN



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RX(22)	RCT	CB 850211-70-0
	RGT	BE 603-35-0 PPh ₃ , BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
	PRO	CD 850211-71-1
RX(23)	RCT	CD 850211-71-1, BE 603-35-0
	PRO	CE 850211-72-2
	CON	100 deg C
	NTE	yield over 11 steps starting from Roche's ester = 27%
RX(27)	RCT	CE 850211-72-2, CN 252342-51-1
	RGT	CA 1070-89-9 (Me ₃ Si) ₂ N.Na
	PRO	AW 850211-74-4
	CON	-78 deg C -> -10 deg C
	NTE	stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

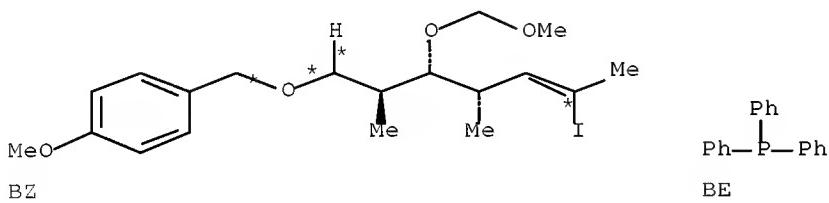
RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

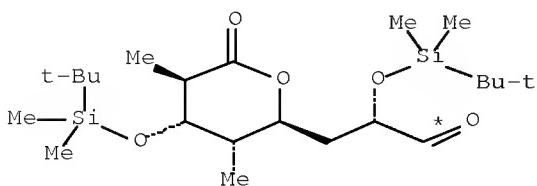
SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

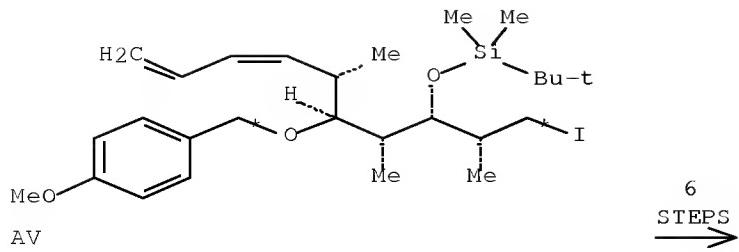
RX(227) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28)
RX(227) BZ + BE + CN + AV ==> CO



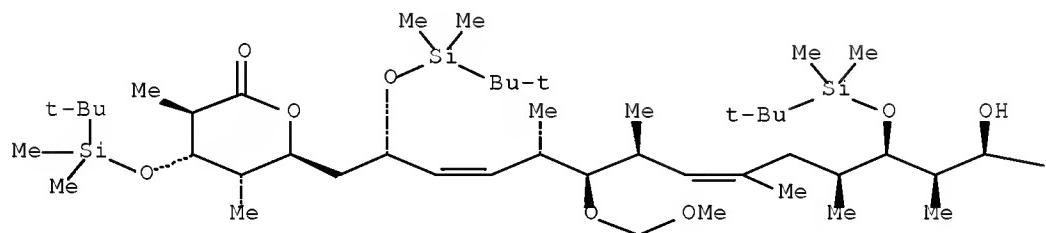
BE



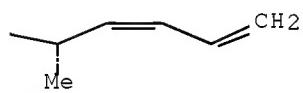
CN



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^{CO}
YIELD 91%

RX(21) RCT BZ 633294-02-7
 RGT CC 84-58-2 DDQ
 PRO CB 850211-70-0
 SOL 7732-18-5 Water

RX(22) RCT CB 850211-70-0
 RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
 PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C

NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

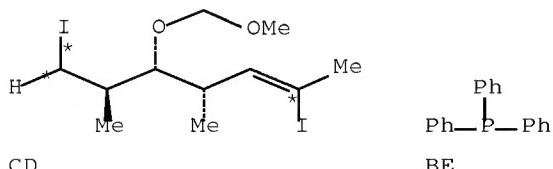
PRO AX 633293-75-1

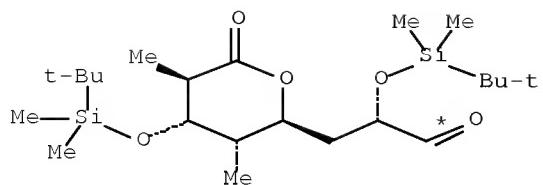
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

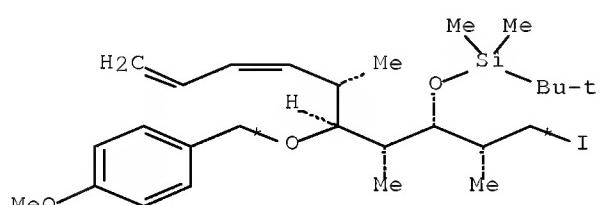
RX(230) OF 354 COMPOSED OF RX(23), RX(27), RX(11), RX(28), RX(29)

RX(230) CD + BE + CN + AV + CP ==> CQ

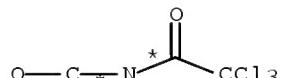




CN



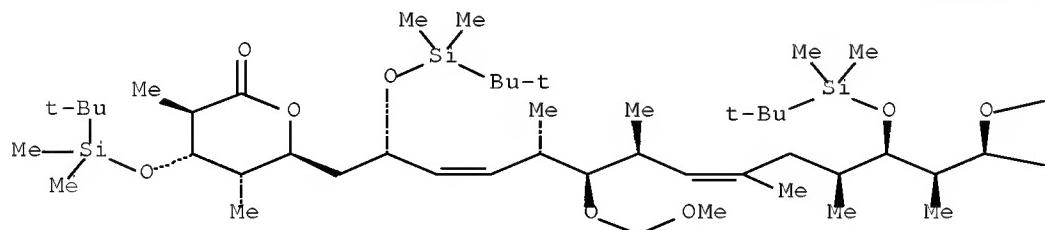
AV

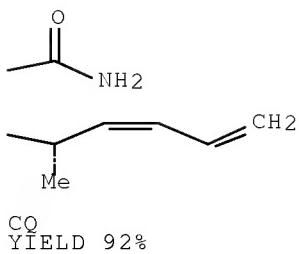


CP

5
STEPS
→

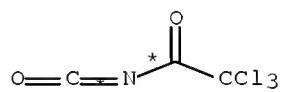
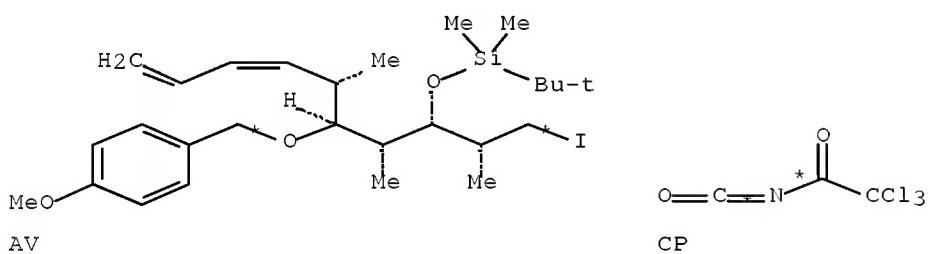
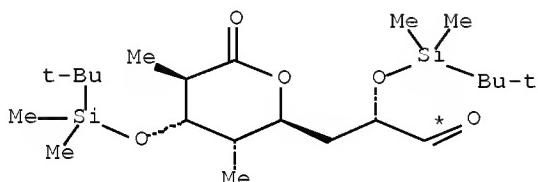
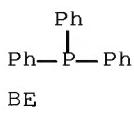
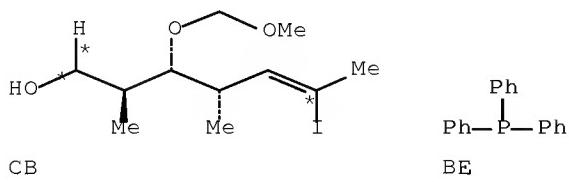
PAGE 1-A





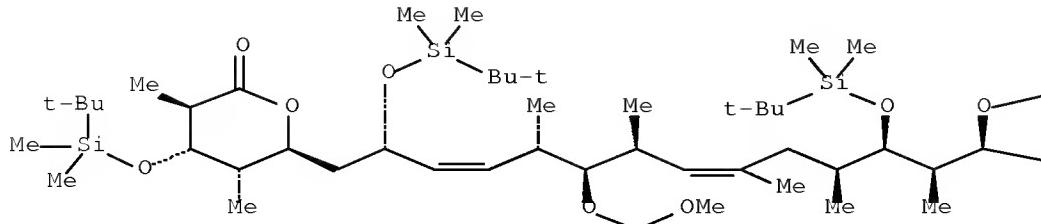
- RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%
- RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
- RX(11) RCT AV 850211-69-7
- STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature
- STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature
- PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling
- RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C
- RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(231) OF 354 COMPOSED OF RX(22), RX(23), RX(27), RX(11), RX(28), RX(29)
RX(231) CB + BE + CN + AV + CP ==> CQ

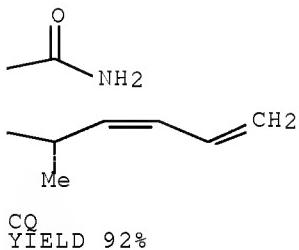


$\xrightarrow{6}$
STEPS

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PAGE 1-B



RX(22) RCT CB 850211-70-0
RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
PRO CE 850211-72-2
CON 100 deg C
NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE (2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

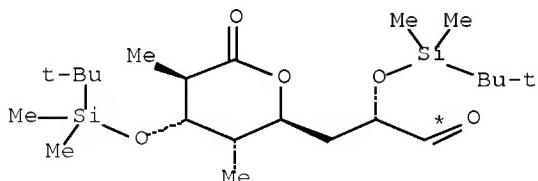
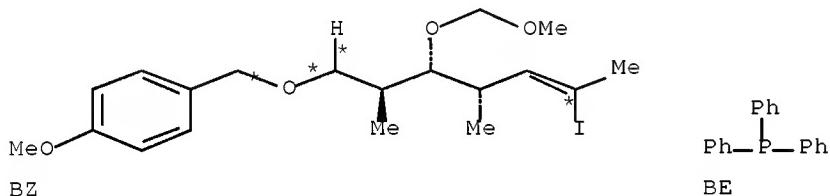
RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

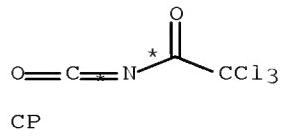
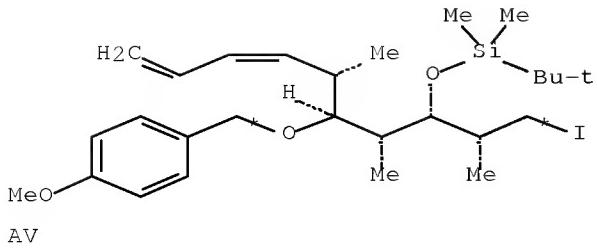
PRO CQ 633293-93-3

RX(232) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28),
 RX(29)

RX(232) BZ + BE + CN + AV + CP ==> CQ

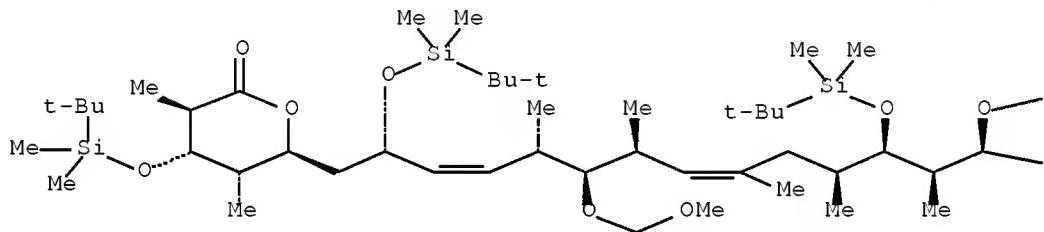


CN

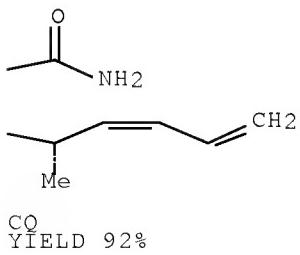


7
STEPS
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RX(21) RCT BZ 633294-02-7
RGD CC 84-58-2 DDQ
PRO CB 850211-70-0
SOL 7732-18-5 Water

RX(22) RCT CB 850211-70-0

RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
 PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

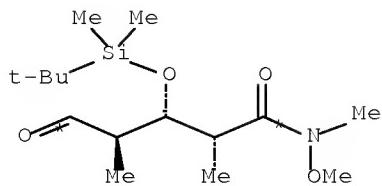
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

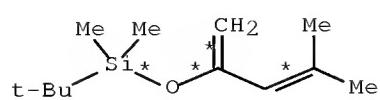
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

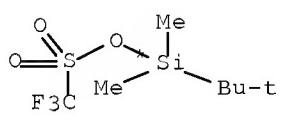
RX(238) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11)
 RX(238) CF + CI + L + CE + AV ==> AX



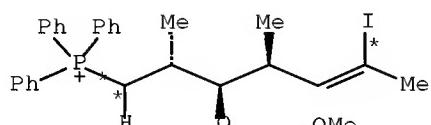
CF



CI



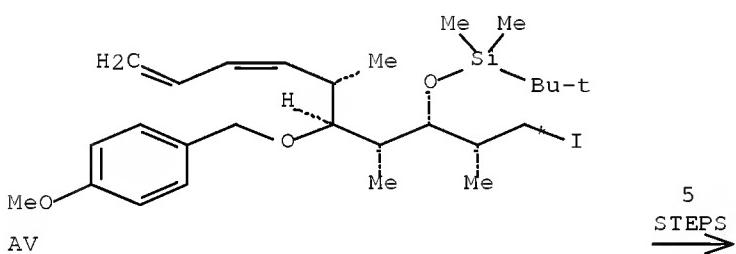
L



P

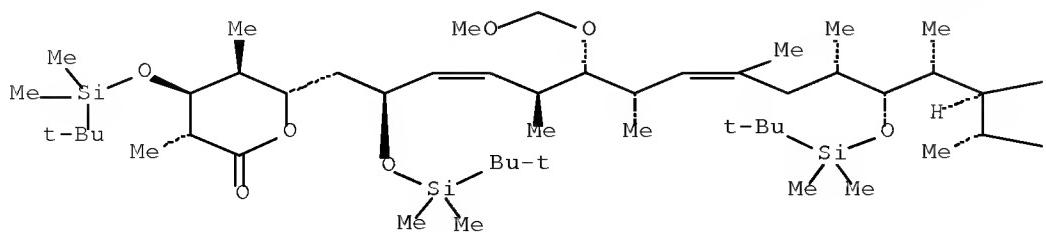
● I⁻

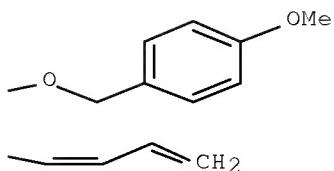
CE



5 STEPS
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AX
YIELD 50%

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

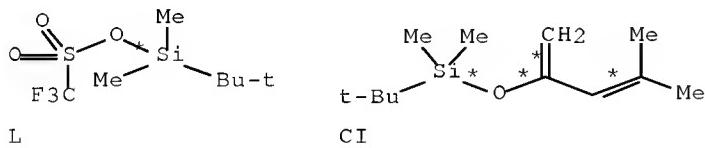
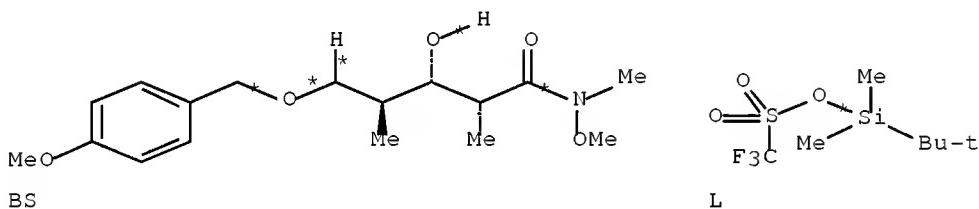
STAGE(2)

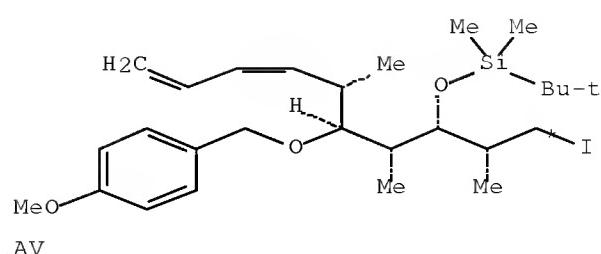
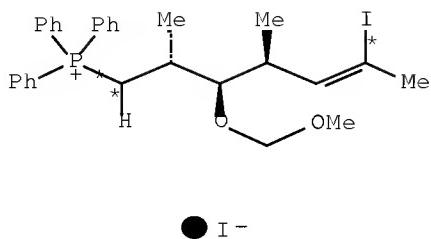
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

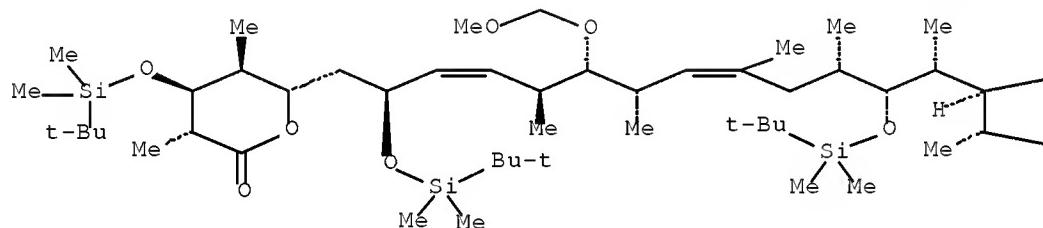
RX(239) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11)
 RX(239) BS + 2 L + CI + CE + AV ==> AX



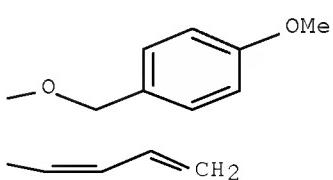


$\xrightarrow[6]{\text{STEPS}}$

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AX
YIELD 50%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2

CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2C12

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2C12

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2C12

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

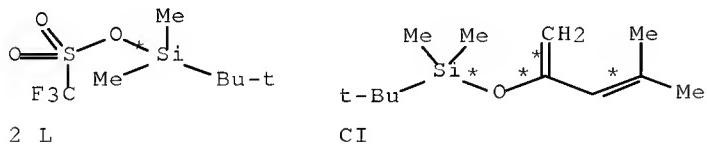
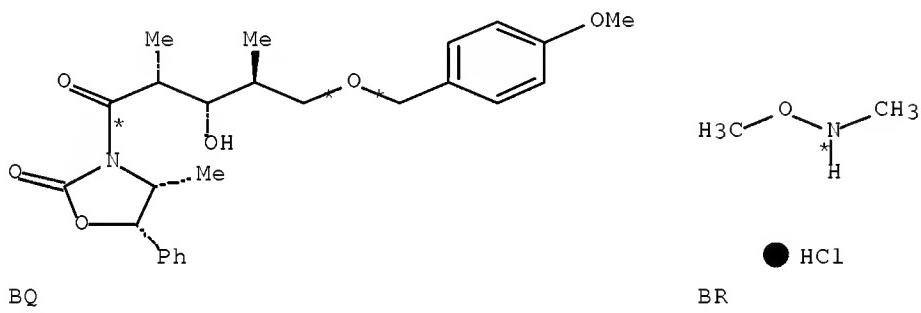
RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

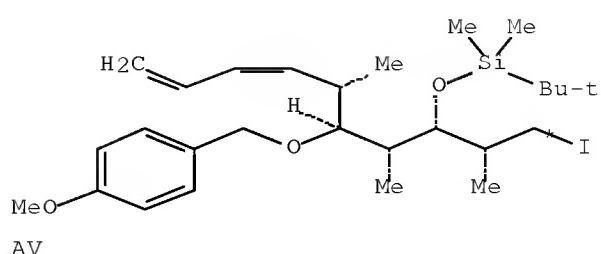
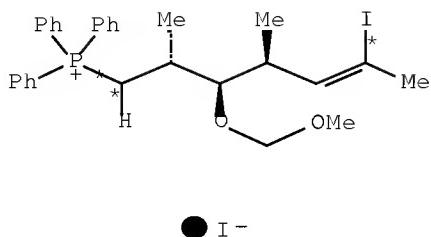
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(240) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
RX(11)

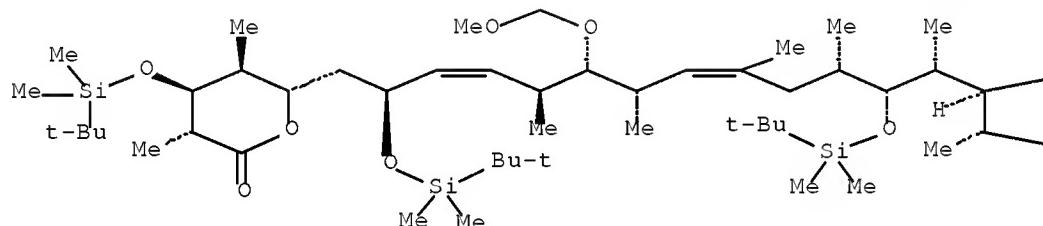
RX(240) BQ + BR + 2 L + CI + CE + AV ==>
AX



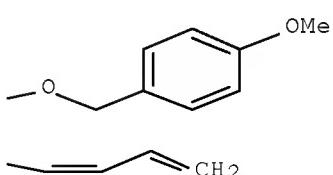


7
STEPS
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AX
YIELD 50%

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

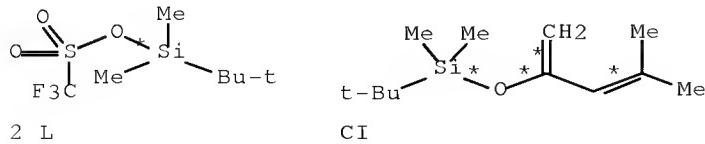
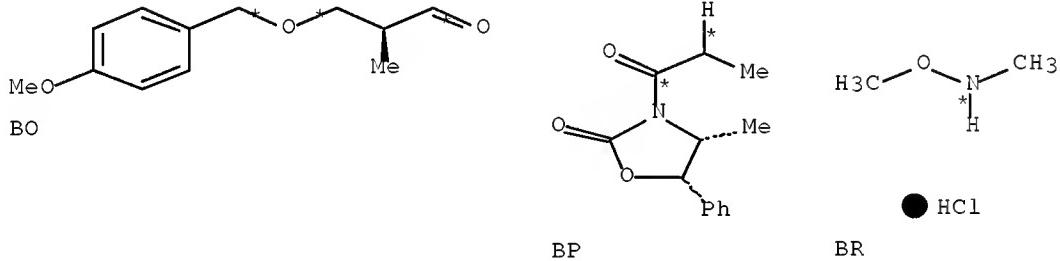
STAGE(2)

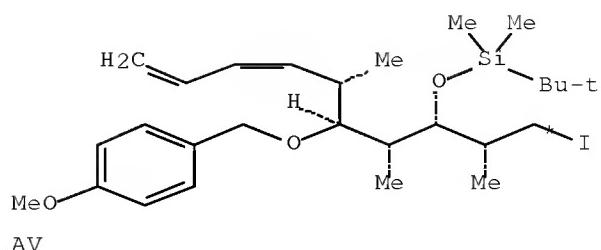
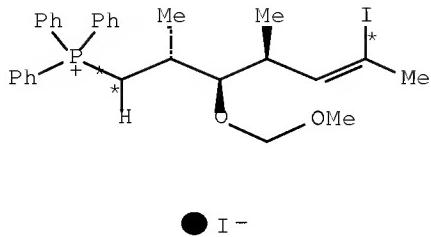
RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

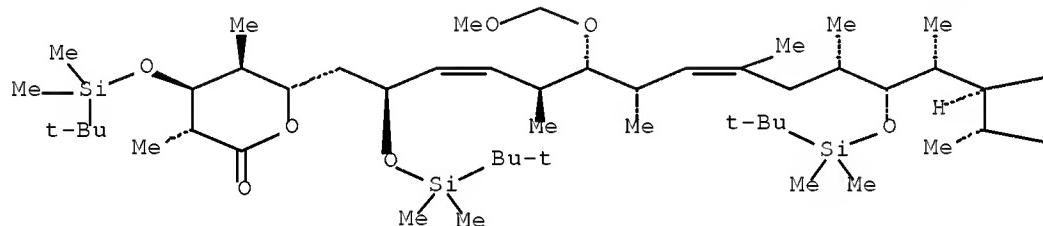
RX(241) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
 RX(27), RX(11)
 RX(241) BO + BP + BR + 2 L + CI + CE + AV
 =====> AX



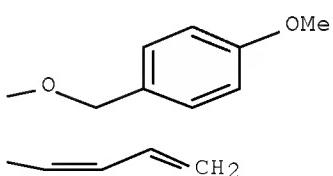


8
STEPS
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AX
YIELD 50%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7

SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

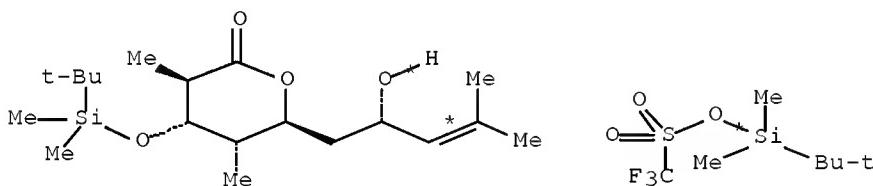
STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

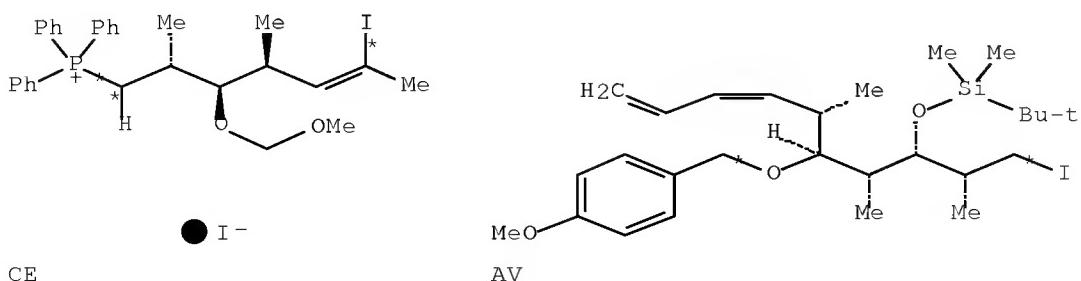
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(242) OF 354 COMPOSED OF RX(26), RX(27), RX(11), RX(28), RX(29)
RX(242) CM + L + CE + AV + CP ==> CQ

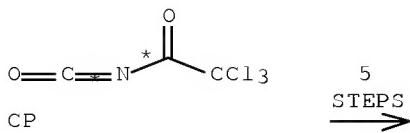


CM L

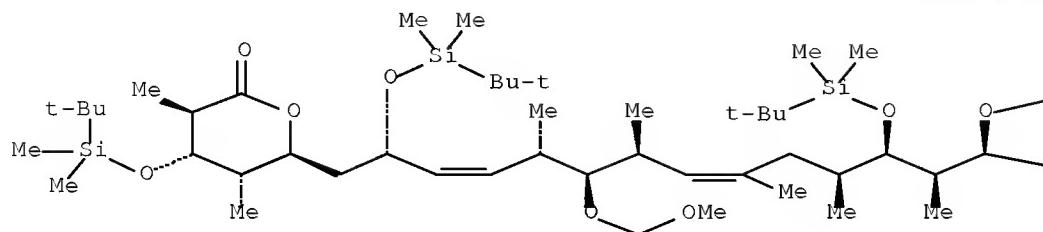


CE

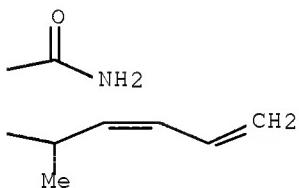
AV



PAGE 1-A



PAGE 1-B



RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂Cl₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
 RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

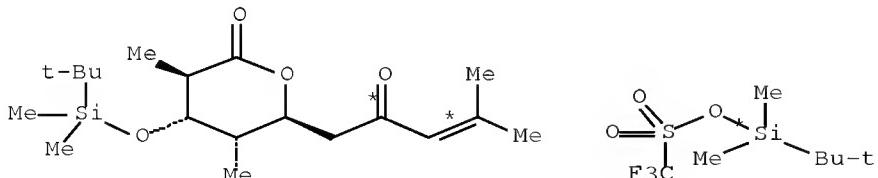
STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

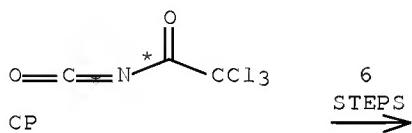
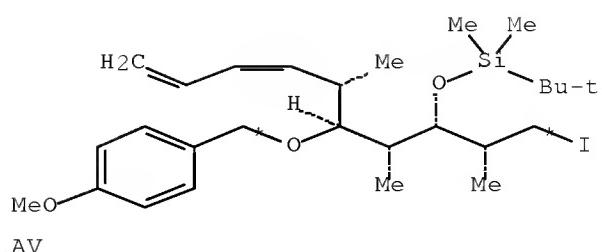
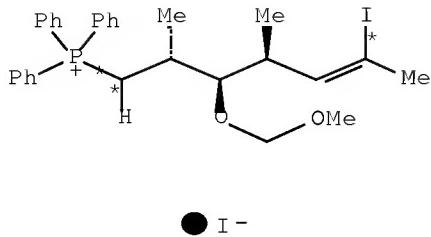
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

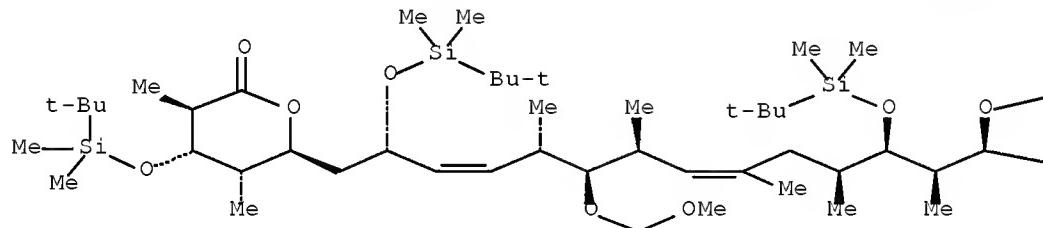
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(243) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)
 RX(243) CJ + L + CE + AV + CP ==> CQ

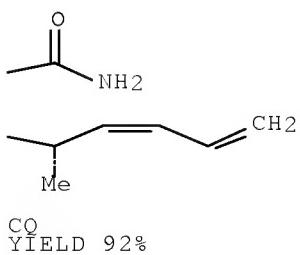




PAGE 1-A



PAGE 1-B



RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH₂C₁₂

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH₂C₁₂

STAGE(3)
 RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

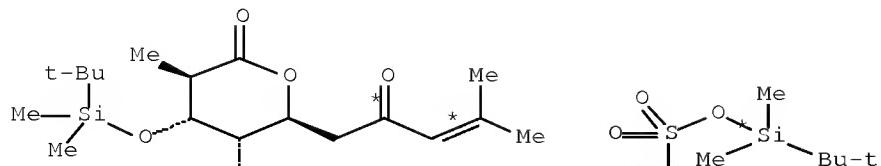
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

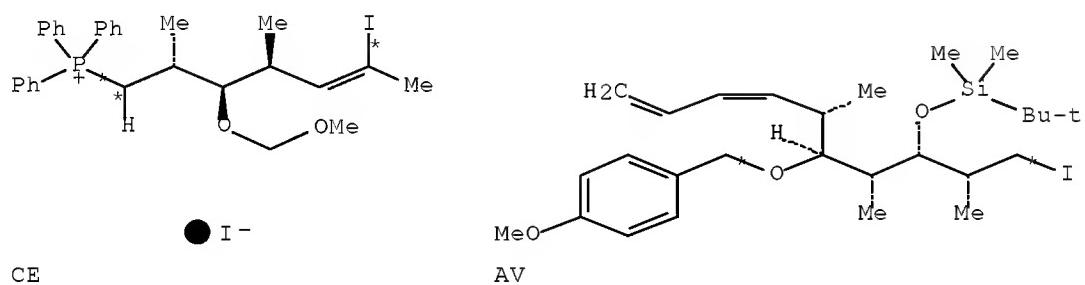
RX(244) OF 354 COMPOSED OF RX(33), RX(26), RX(27), RX(11), RX(28)

RX(244) CJ + L + CE + AV ==> CO



CJ

L

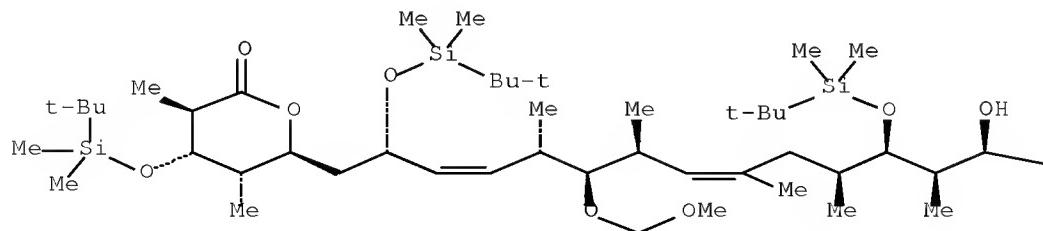


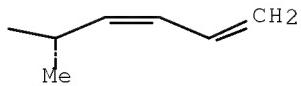
CE

AV

5
STEPS
→

PAGE 1-A





CO
YIELD 91%

- RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1
- RX(26) RCT CM 256920-77-1, L 69739-34-0
- STAGE(1)
 SOL 75-09-2 CH₂Cl₂
- STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH₂Cl₂
- STAGE(3)
 RGT BE 603-35-0 PPh₃
- PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%
- RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%
- RX(11) RCT AV 850211-69-7
- STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature
- STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

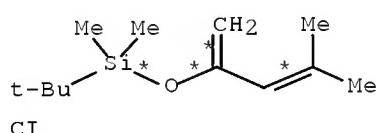
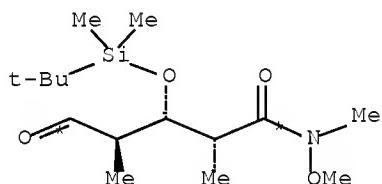
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

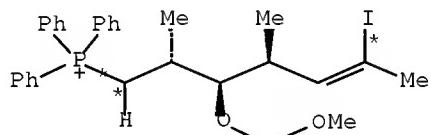
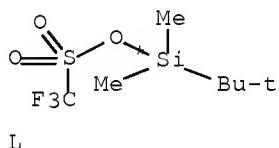
CON 0 - room temperature deg C

RX(245) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28),
RX(29)

RX(245) CF + CI + L + CE + AV + CP ==>
CO₂



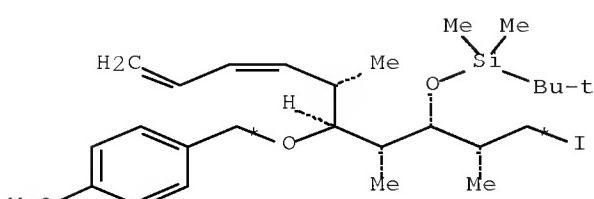
CF



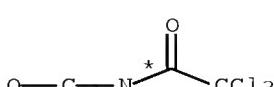
L



CE



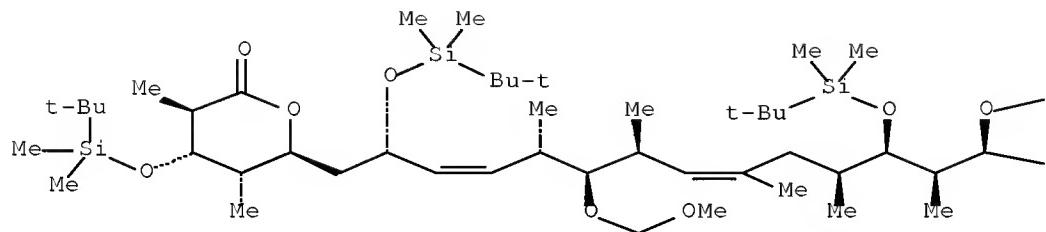
AV



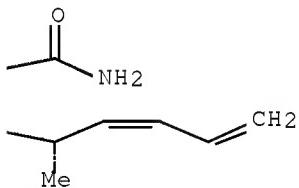
CP

7
STEPS
→

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CO
YIELD 92%

RX(25) RCT CF 252342-42-0

STAGE (1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE (2)
RCT CI 130043-07-1
CON -78 deg C

STAGE (3)
RGT CL 76-05-1 F3CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH₂Cl₂

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH₂Cl₂

STAGE(3)
 RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

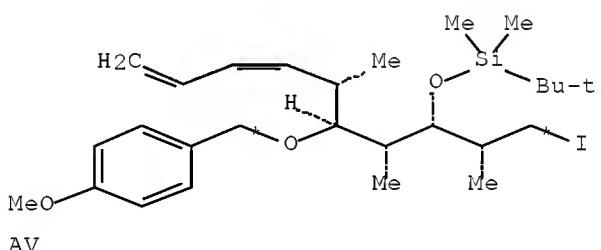
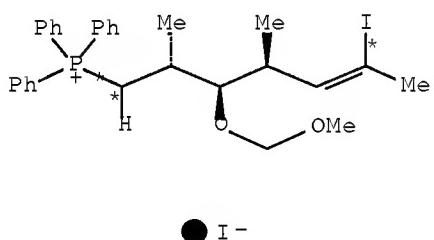
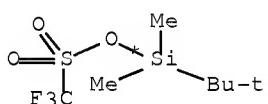
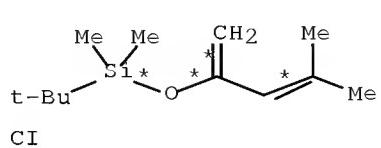
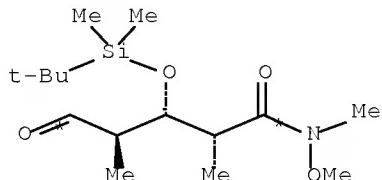
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3

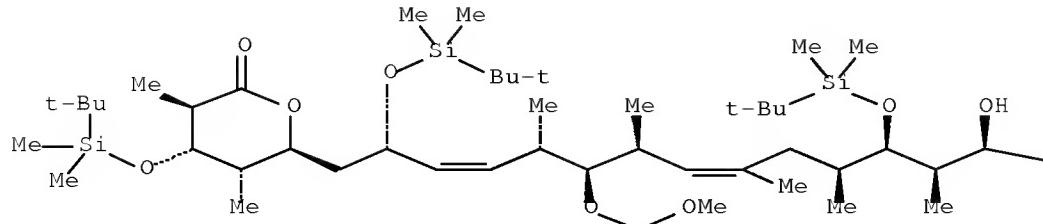
PRO CQ 633293--93--3

RX(246) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28)
RX(246) CF + CI + L + CE + AV ==> CO

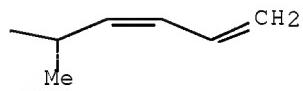


6
STEPS

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PAGE 1-B



CO
YIELD 91%

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂C₁₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE (3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

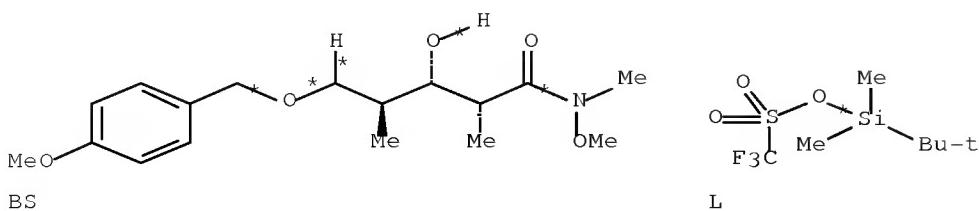
STAGE (2)
RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

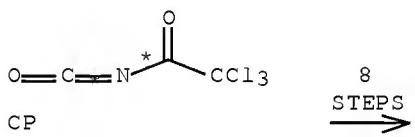
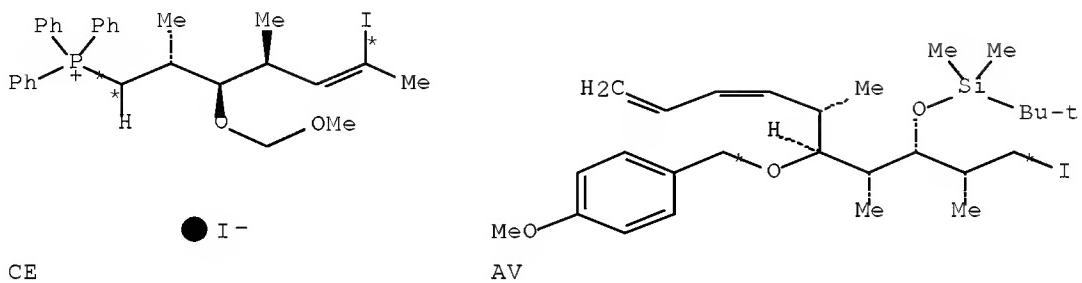
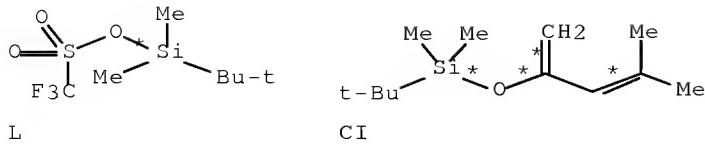
PRO AX 633293-75-1
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

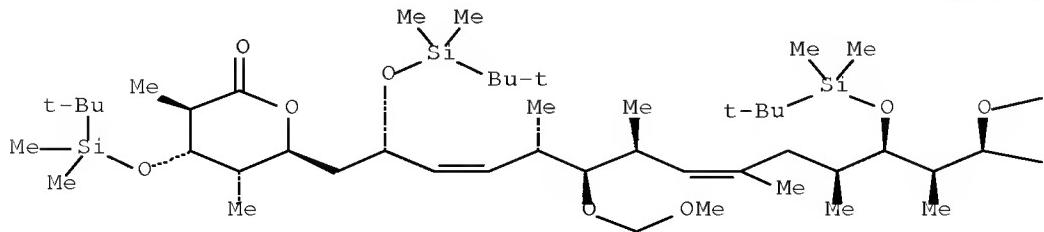
RX(247) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
RX(28), RX(29)

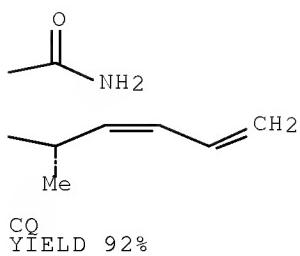
RX(247) BS + 2 L + CI + CE + AV + CP ==>
CQ





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RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,

[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

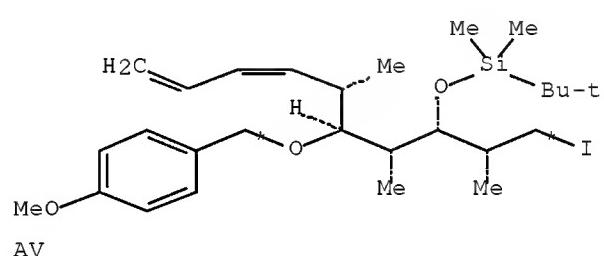
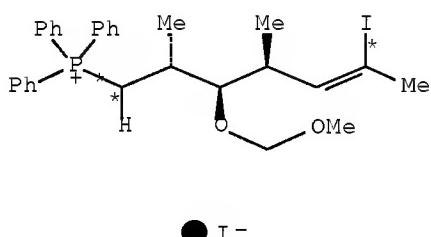
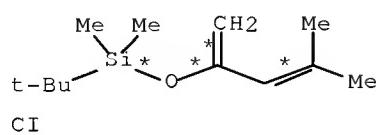
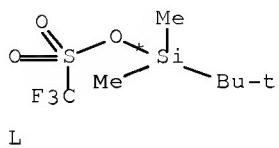
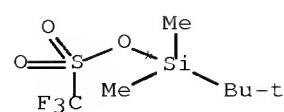
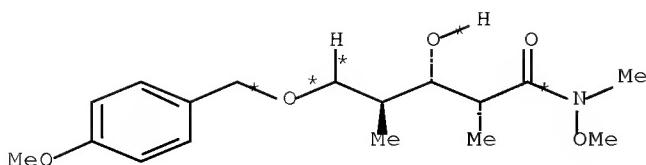
RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al₂O₃

PRO CQ 633293-93-3

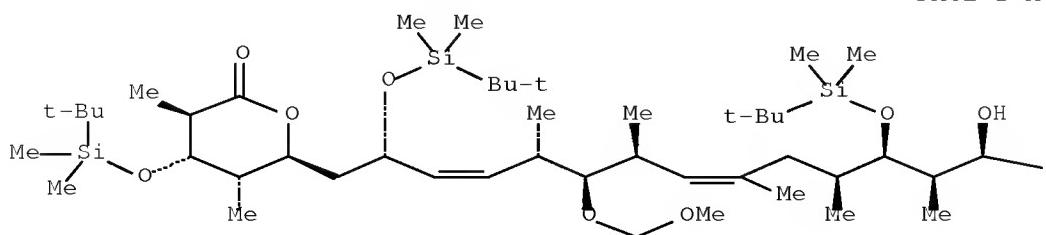
RX(248) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
RX(28)

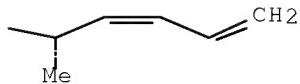
RX(248) BS + 2 L + CI + CE + AV ==> CO



7
STEPS
→

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^{CO}
YIELD 91%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2Cl2

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

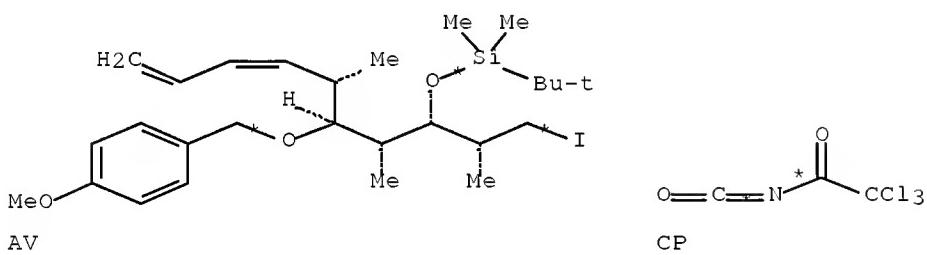
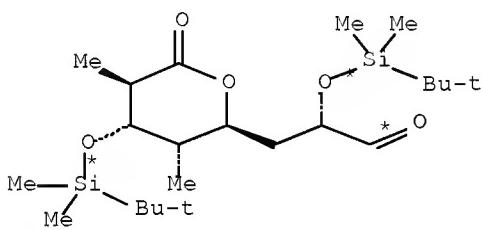
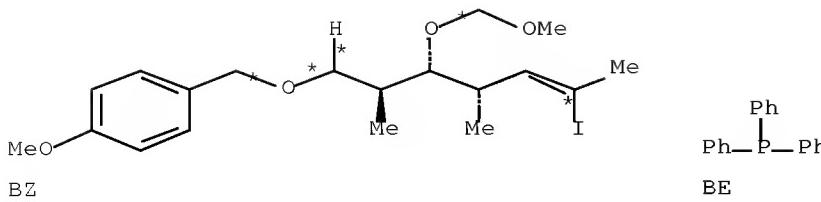
PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

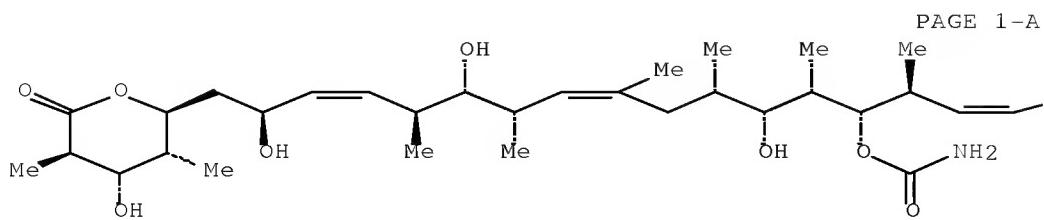
CON 0 - room temperature deg C

RX(249) OF 354 COMPOSED OF RX(21), RX(22), RX(23), RX(27), RX(11), RX(28),
RX(29), RX(30)

RX(249) BZ + BE + CN + AV + CP ==> CS



8
STEPS



 CH₂

CS
YIELD 95%

RX(21) RCT BZ 633294-02-7
 RGT CC 84-58-2 DDQ
 PRO CB 850211-70-0
 SOL 7732-18-5 Water

RX(22) RCT CB 850211-70-0
 RGT BE 603-35-0 PPh₃, BF 7553-56-2 I2, BG 288-32-4 1H-Imidazole
 PRO CD 850211-71-1

RX(23) RCT CD 850211-71-1, BE 603-35-0
 PRO CE 850211-72-2
 CON 100 deg C
 NTE yield over 11 steps starting from Roche's ester = 27%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

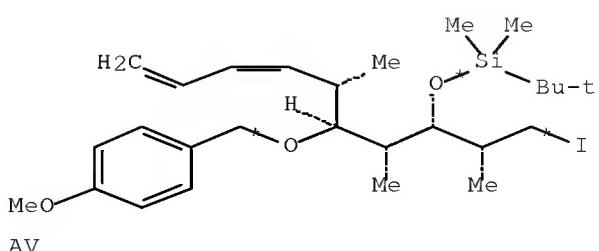
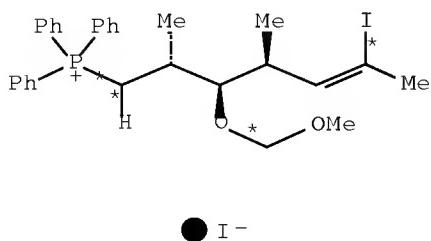
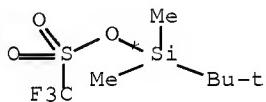
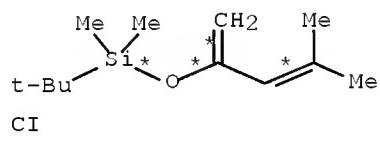
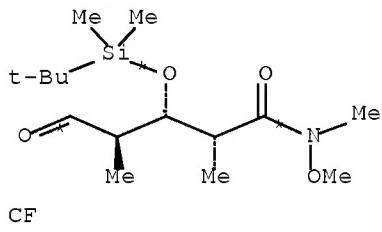
RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

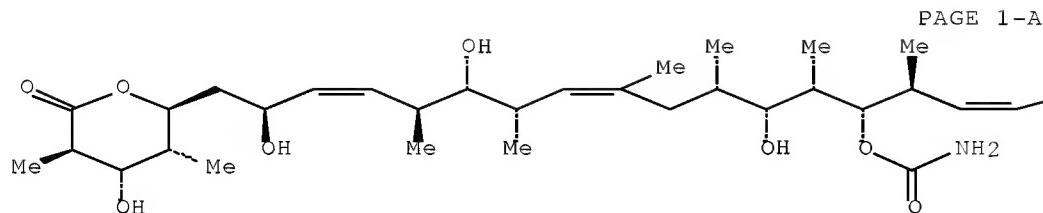
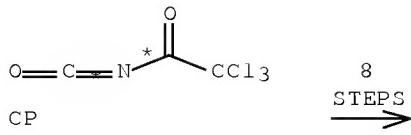
RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(250) OF 354 COMPOSED OF RX(25), RX(33), RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

RX(250) CF + CI + L + CE + AV + CP ==>
CS





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CS
YIELD 95%

RX(25) RCT CF 252342-42-0

STAGE (1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE (2)

RCT CI 130043-07-1
CON -78 deg C

STAGE (3)

RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al₂O₃

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

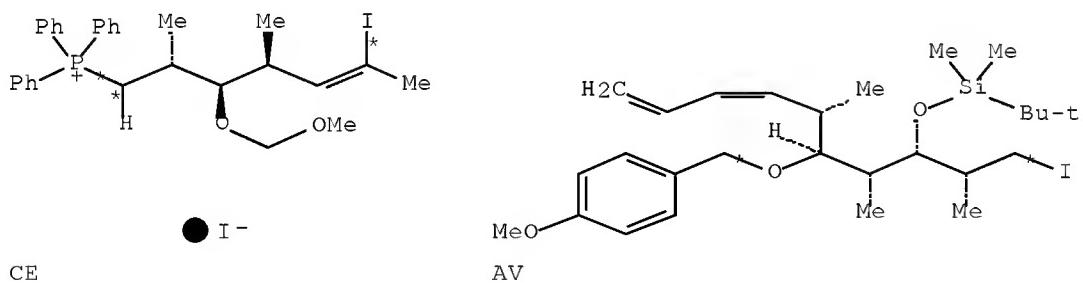
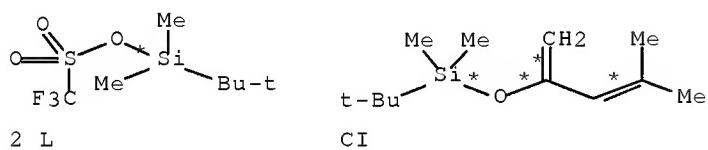
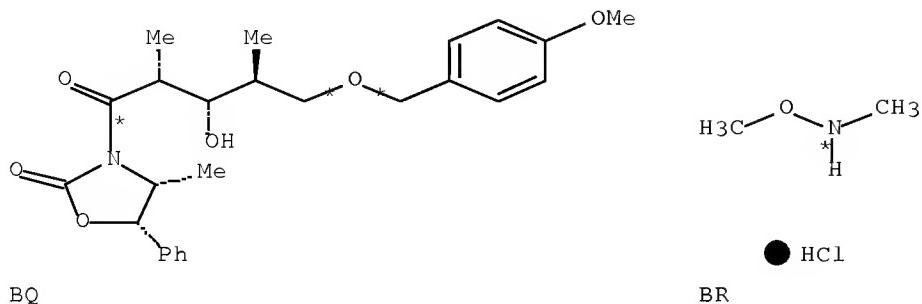
PRO CS 127943-53-7

SOL 7732-18-5 Water, 67-56-1 MeOH

NTE overall yield via iodine substituted pyran-2-one intermediate =

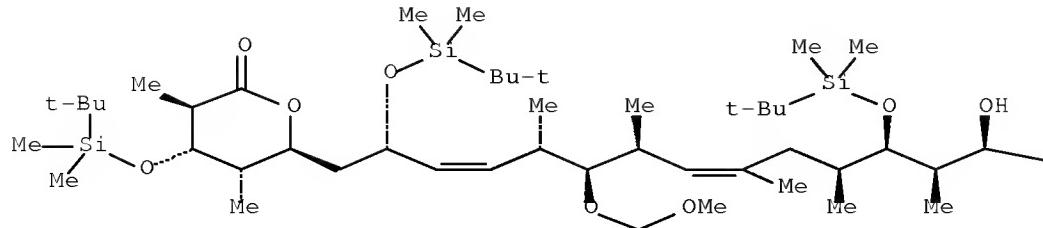
10%

RX(252) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
RX(11), RX(28)
RX(252) BQ + BR + 2 L + CI + CE + AV ==>
CO

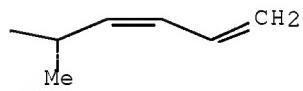


8
STEPS
→

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CO
YIELD 91%

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1

CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH2C12

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2C12

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

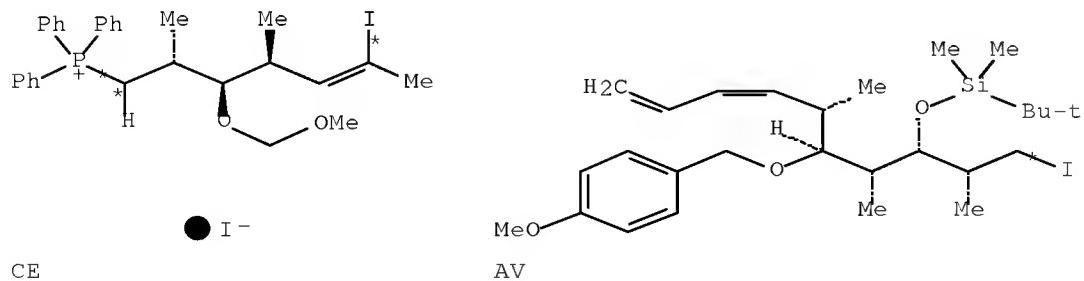
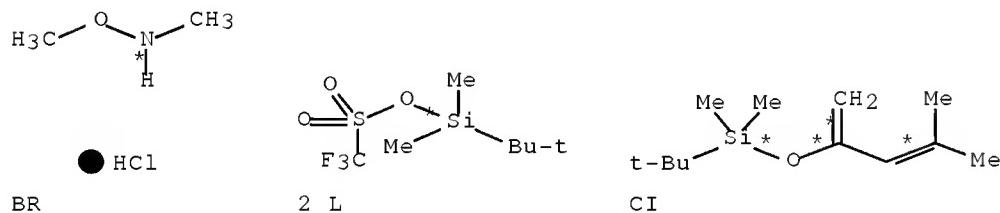
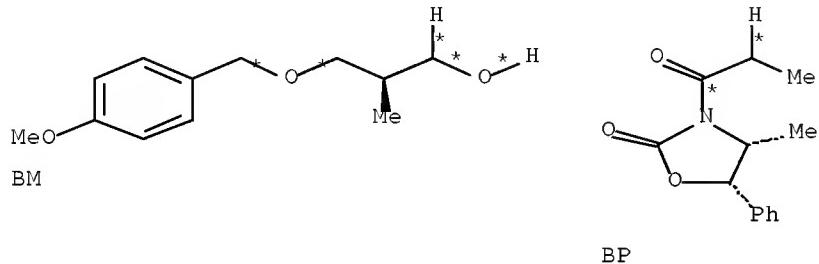
RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

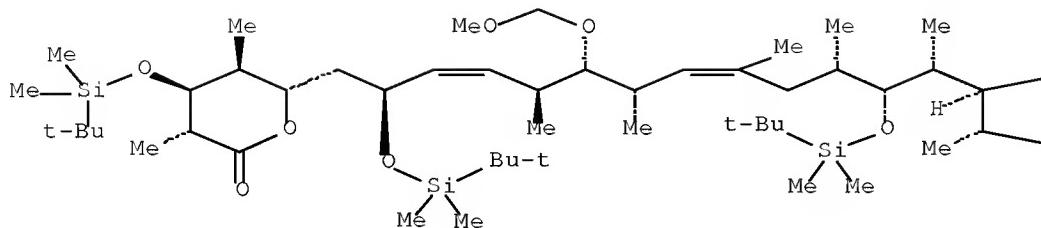
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(304) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
 RX(26), RX(27), RX(11)
 RX(304) BM + BP + BR + 2 L + CI + CE + AV
 ==> ΔX

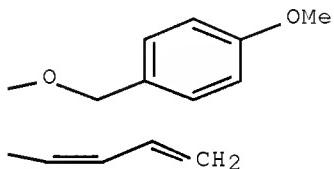


9
STEPS
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PAGE 1-B



^{AX}
YIELD 50%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F3CSO₃BBu₂
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂

CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2C12

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2C12

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2C12

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C → room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

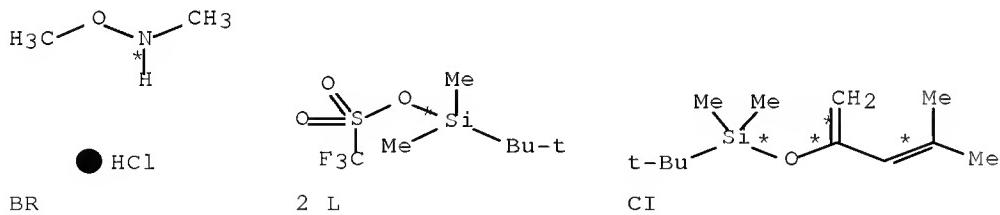
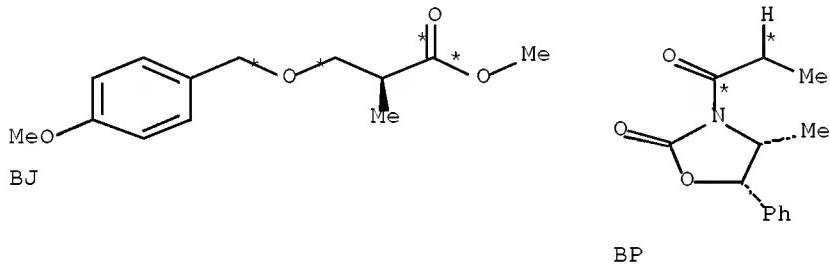
RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

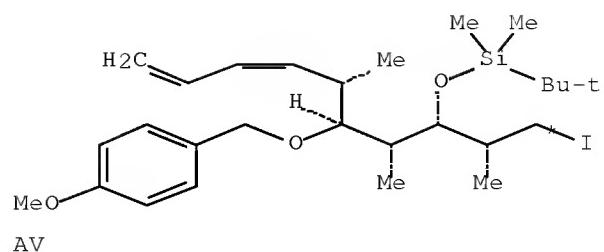
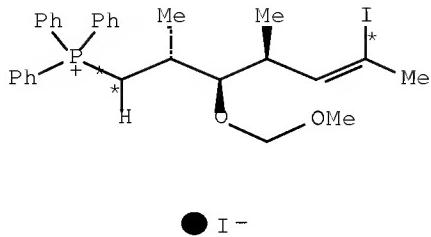
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(306) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
RX(33), RX(26), RX(27), RX(11)

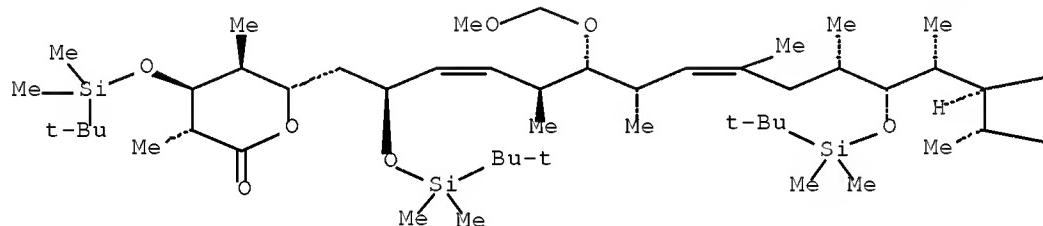
RX(306) BJ + BP + BR + 2 L + CI + CE + AV
====> AX



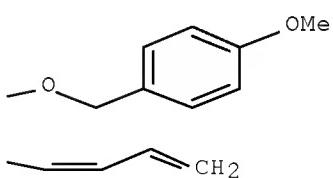


10
STEPS
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AX
YIELD 50%

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9

NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
 PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

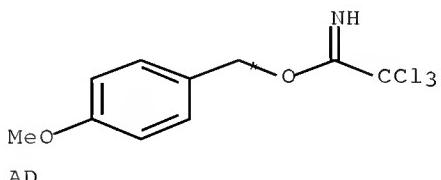
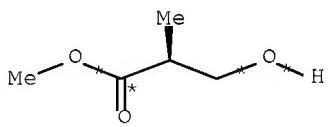
CON 20 hours, room temperature

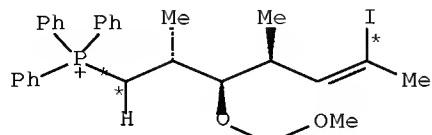
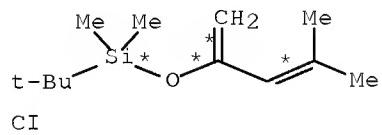
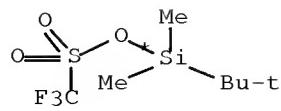
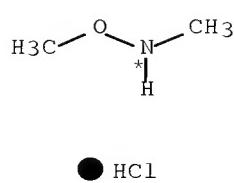
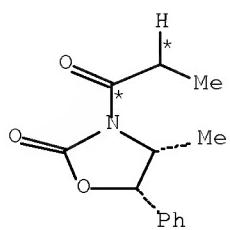
PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(308) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
RX(25), RX(33), RX(26), RX(27), RX(11)

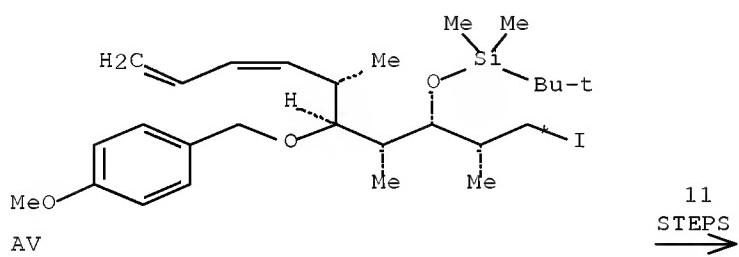
RX(308) BI + AD + BP + BR + 2 L + CI + CE +
AV ==> AX



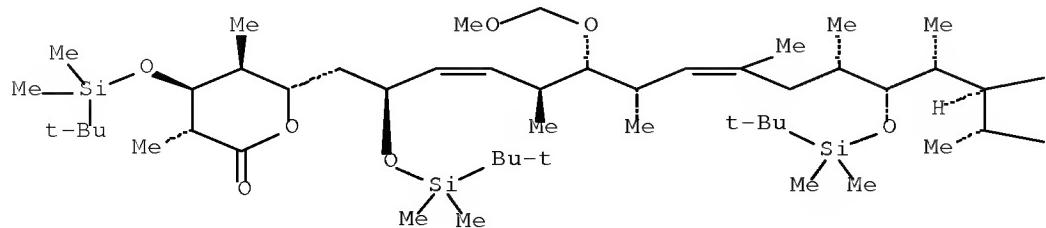


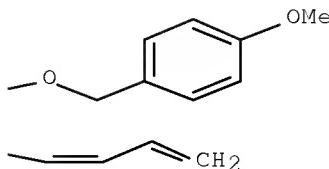
● I⁻

CE



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^{AX}
YIELD 50%

RX(13) RCT BI 80657-57-4, AD 89238-99-3
RGT BK 24057-28-1 Pyridinium tosylate
PRO BJ 132969-71-2
SOL 75-09-2 CH₂C₁₂, 110-82-7 Cyclohexane

RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F₃CSO₃BBu₂
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

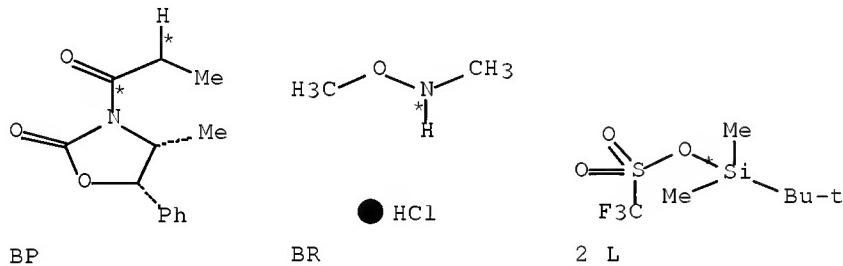
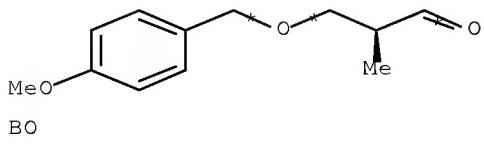
STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki

coupling

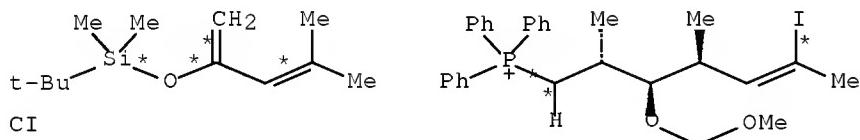
RX(310) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28)
RX(310) BO + BP + BR + 2 L + CI + CE + AV
====> CO



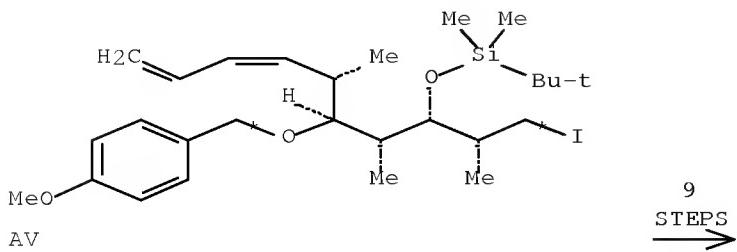
BR



2 L

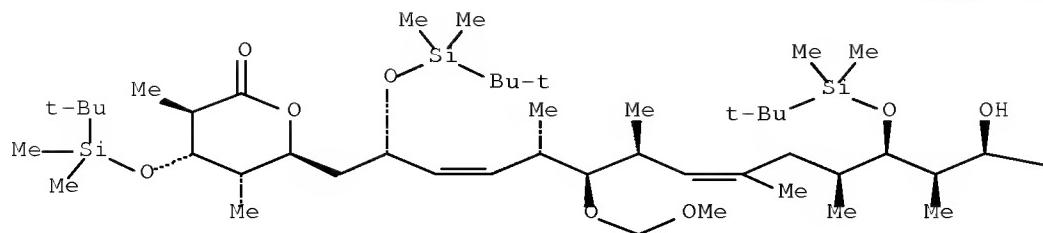


CE



9
STEPS

PAGE 1-A



PAGE 1-B



^{CO}
YIELD 91%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F3CSO₃BBu₂
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)

RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE(2)

RCT CI 130043-07-1
CON -78 deg C

STAGE(3)

RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1

RGT CW 54575-49-4 K Selectride

PRO CM 256920-77-1

SOL 109-99-9 THF, 108-88-3 PhMe

NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)

SOL 75-09-2 CH₂Cl₂

STAGE(2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE(3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)₂N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,

[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,

(SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

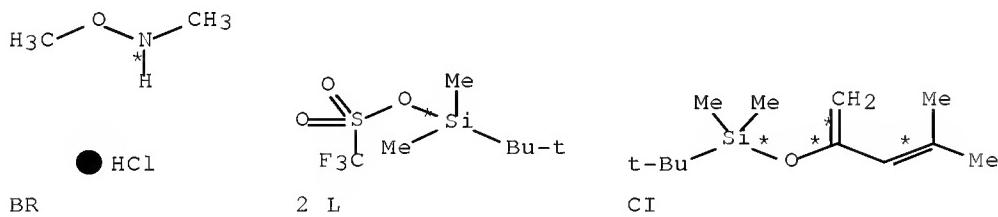
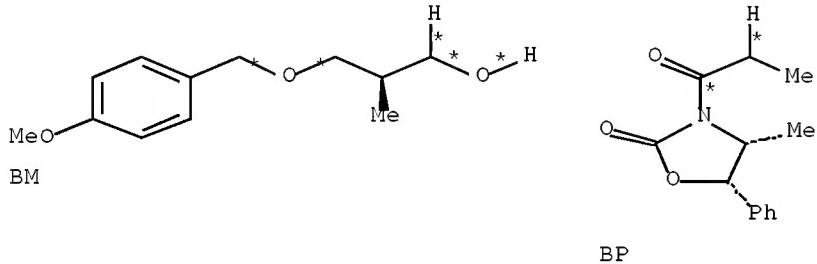
PRO CO 633293-76-2

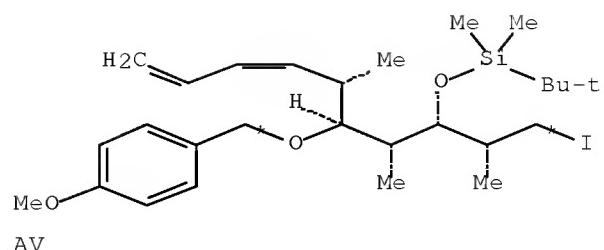
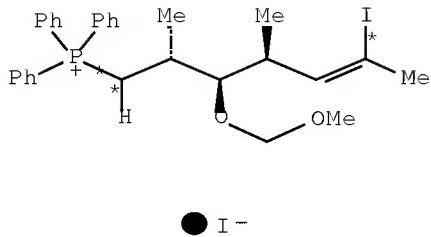
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

RX(312) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
 RX(26), RX(27), RX(11), RX(28)

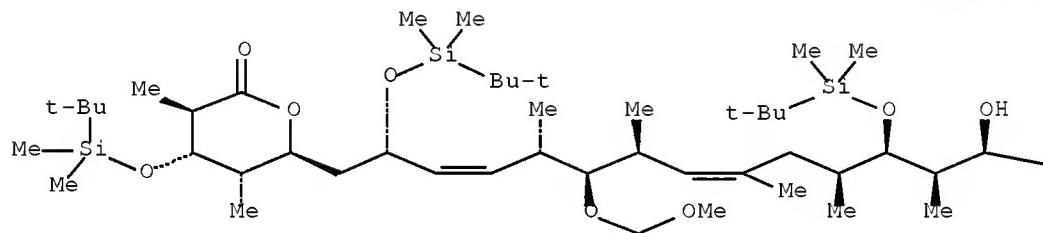
RX(312) BM + BP + BR + 2 L + CI + CE + AV
 ==> CO



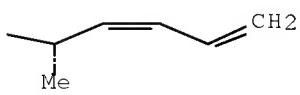


10
STEPS
→

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PAGE 1-B



CO
YIELD 91%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4

RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

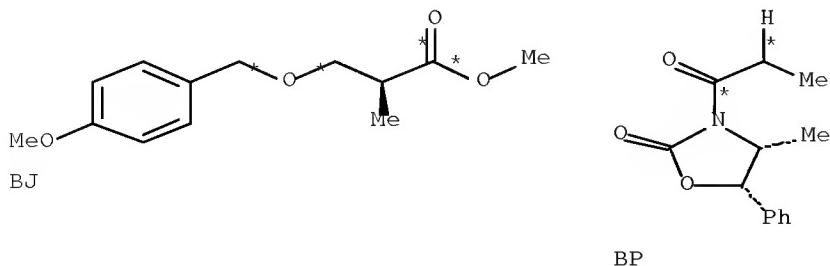
PRO AX 633293-75-1

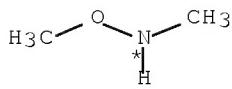
NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

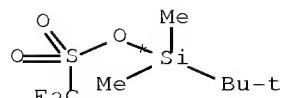
RX(314) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
RX(33), RX(26), RX(27), RX(11), RX(28)

RX(314) BJ + BP + BR + 2 L + CI + CE + AV
====> CO

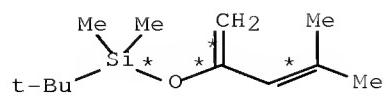




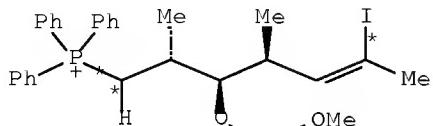
BR



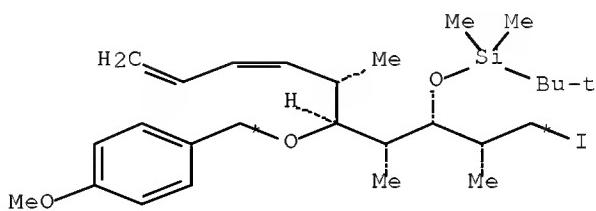
2 L



CI



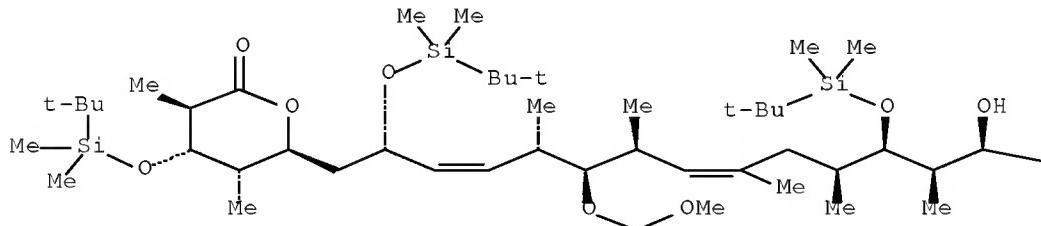
CE

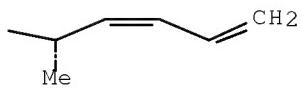


AV

11
STEPS
→

PAGE 1-A





^{CO}
YIELD 91%

- RX(14) RCT BJ 132969-71-2
 RGT BN 16853-85-3 LiAlH₄
 PRO BM 136320-64-4
 SOL 109-99-9 THF
- RX(15) RCT BM 136320-64-4
 PRO BO 132969-60-9
 NTE Swern oxidation
- RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et₃N, F 60669-69-4 F3CSO₃BBu₂
 PRO BQ 132969-62-1
- RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%
- RX(24) RCT BS 252342-49-7, L 69739-34-0
- STAGE(1)
 RGT N 108-48-5 2,6-Lutidine
- STAGE(2)
 RGT CG 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂
 SOL 64-17-5 EtOH
- STAGE(3)
 RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂
- PRO CF 252342-42-0
- RX(25) RCT CF 252342-42-0
- STAGE(1)
 RGT CK 7550-45-0 TiCl₄
 SOL 75-09-2 CH₂C₁₂
- STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

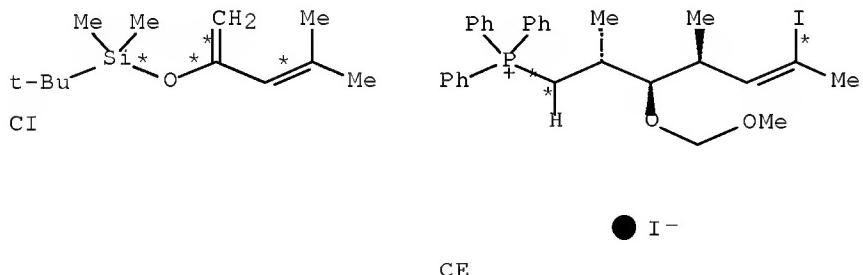
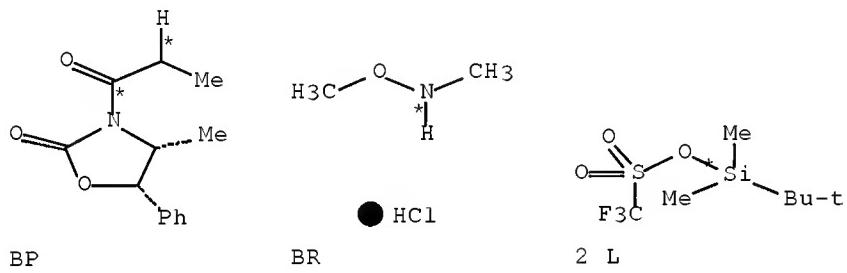
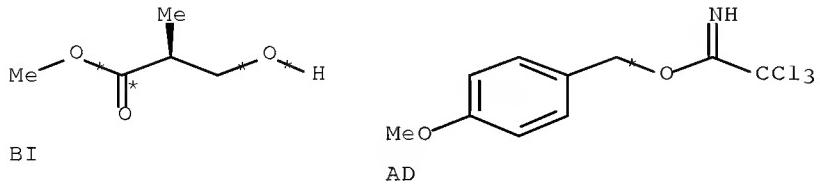
STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

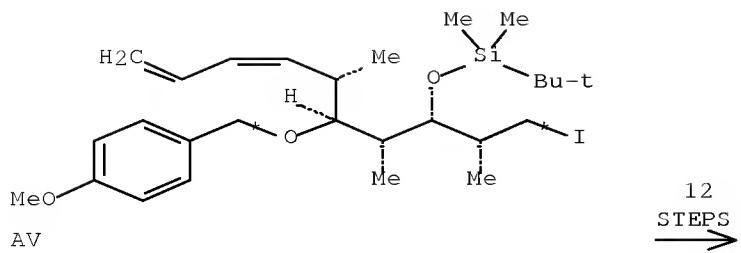
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ

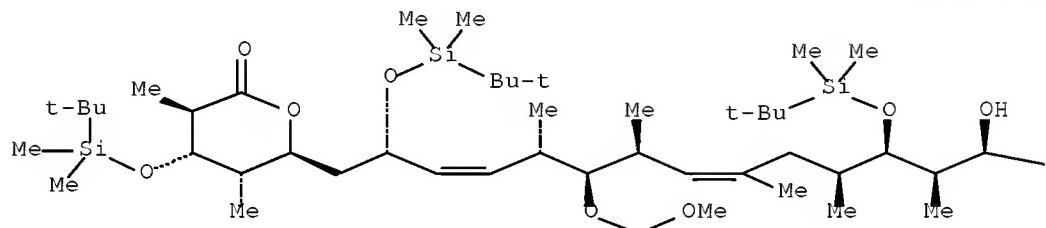
PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(316) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28)
 RX(316) BI + AD + BP + BR + 2 L + CI + CE +
 AV ==> CO

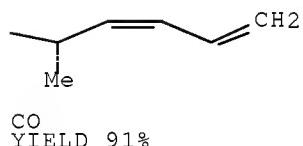




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RX(13) RCT BI 80657-57-4, AD 89238-99-3
 RGT BK 24057-28-1 Pyridinium tosylate
 PRO BJ 132969-71-2
 SOL 75-09-2 CH₂Cl₂, 110-82-7 Cyclohexane

RX(14) RCT BJ 132969-71-2
 RGT BN 16853-85-3 LiAlH₄
 PRO BM 136320-64-4
 SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
 PRO BO 132969-60-9
 NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2C12

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2C12

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2C12

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE (2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

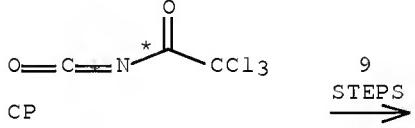
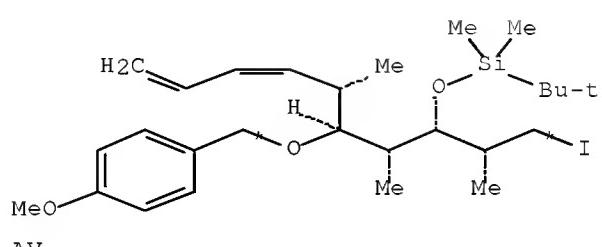
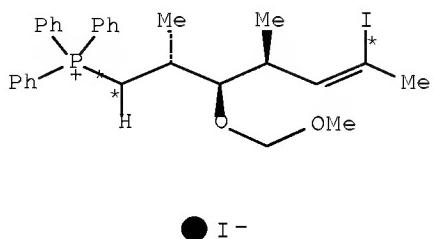
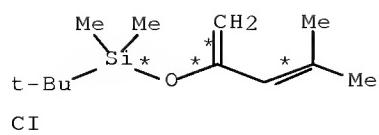
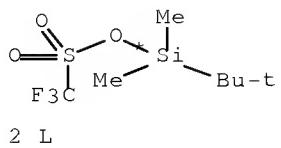
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(318) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
 RX(11), RX(28), RX(29)
 RX(318) BQ + BR + 2 L + CI + CE + AV + CP
 ==> CQ

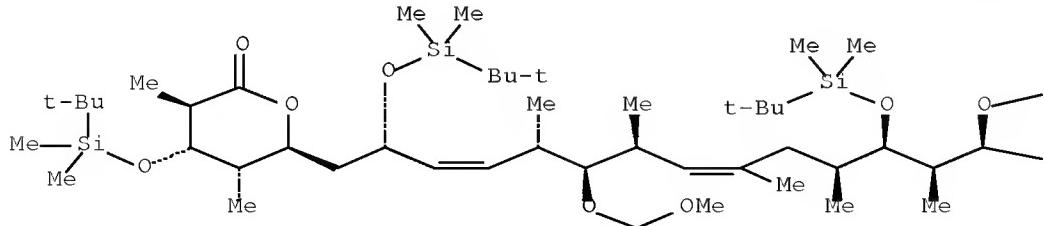
BQ

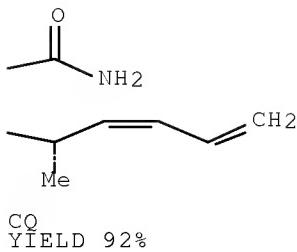
BR

● HCl



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RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl₄
 SOL 75-09-2 CH₂C₁₂

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F₃CCO₂H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me₃Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs₂CO₃

CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂C₁₂

CON 0 - room temperature deg C

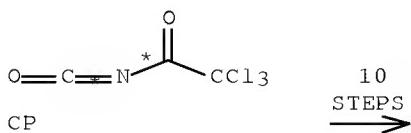
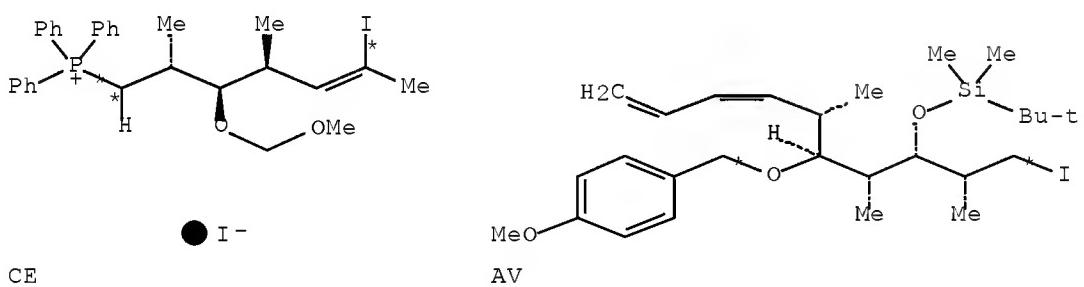
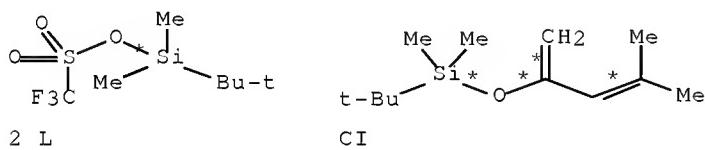
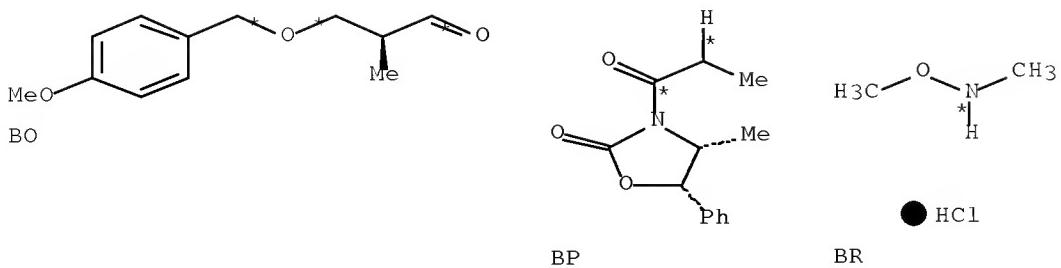
RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al₂O₃

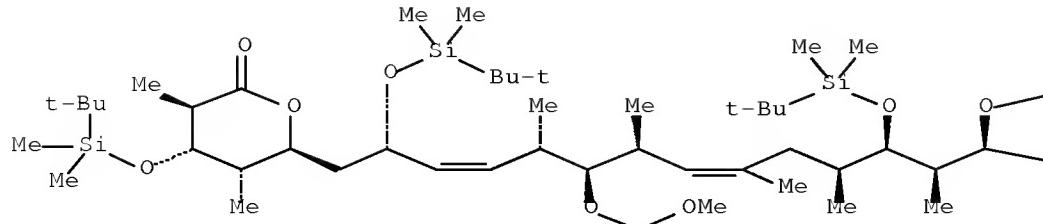
PRO CQ 633293-93-3

RX(320) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28), RX(29)

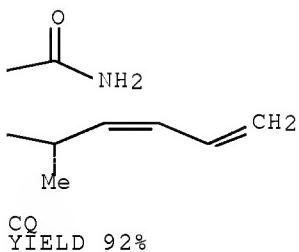
RX(320) BO + BP + BR + 2 L + CI + CE + AV +
CP ==> CQ



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CO₂
YIELD 92%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4

SOL 75-09-2 CH₂C₁₂

STAGE (2)

RCT CI 130043-07-1
CON -78 deg C

STAGE (3)

RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE (1)

SOL 75-09-2 CH₂C₁₂

STAGE (2)

RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE (3)

RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE (2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs₂CO₃
CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

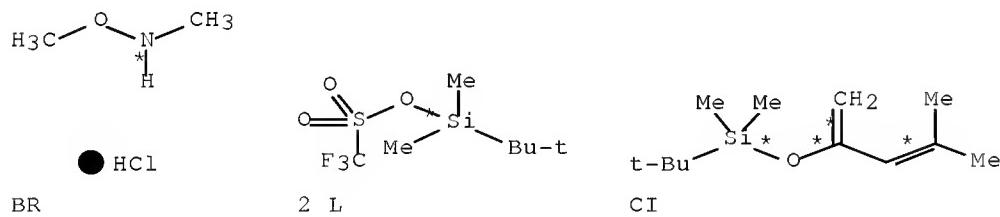
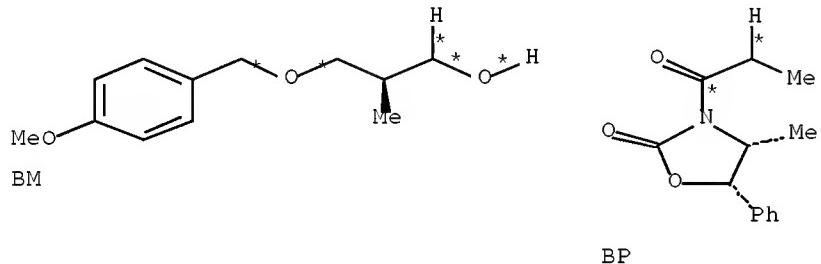
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

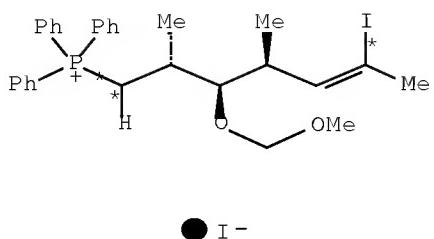
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al₂O₃
PRO CQ 633293-93-3

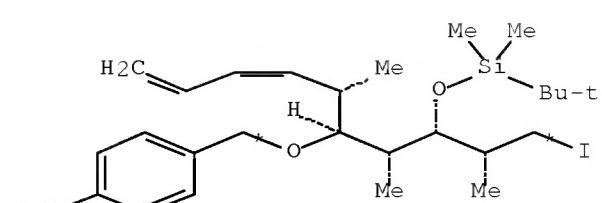
RX(322) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
RX(26), RX(27), RX(11), RX(28), RX(29)

RX(322) BM + BP + BR + 2 L + CI + CE + AV +
CP ==> CQ

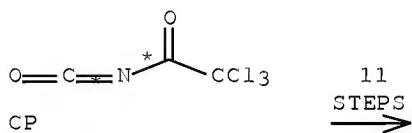




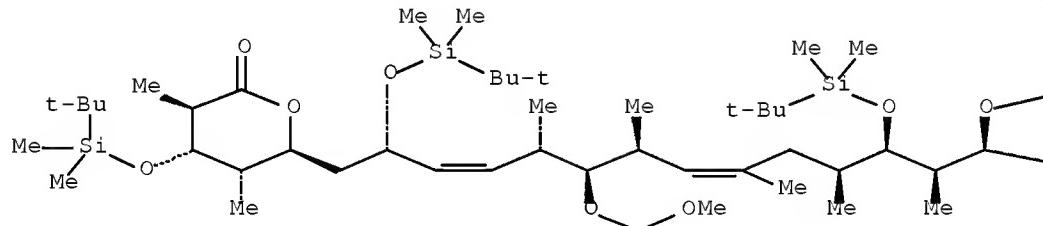
CE



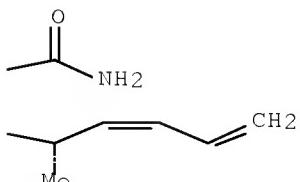
AV



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C_Q
YIELD 92%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9

NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
 PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe3
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
 RGT N 108-48-5 2,6-Lutidine

STAGE(2)
 RGT CG 1333-74-0 H2
 CAT 12135-22-7 Pd(OH)2
 SOL 64-17-5 EtOH

STAGE(3)
 RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
 RGT CK 7550-45-0 TiCl4
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1

NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1

RGT CA 1070-89-9 (Me3Si)2N.Na

PRO AW 850211-74-4

CON -78 deg C -> -10 deg C

NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C

SUBSTAGE(2) -78 deg C

SUBSTAGE(3) -78 deg C -> room temperature

SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

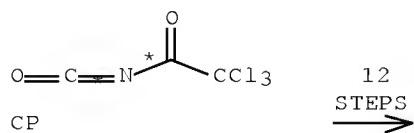
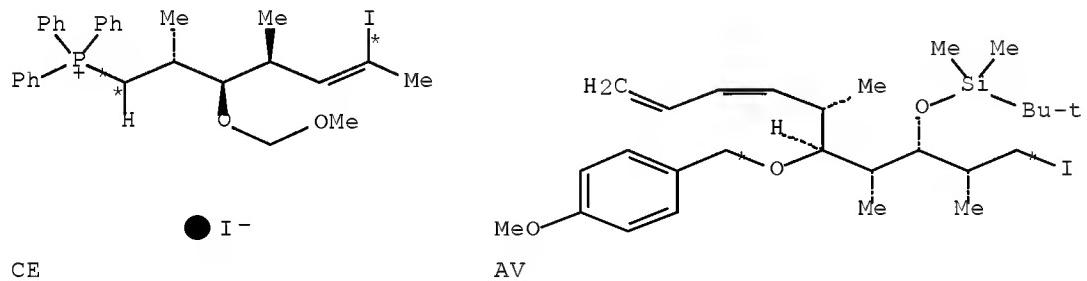
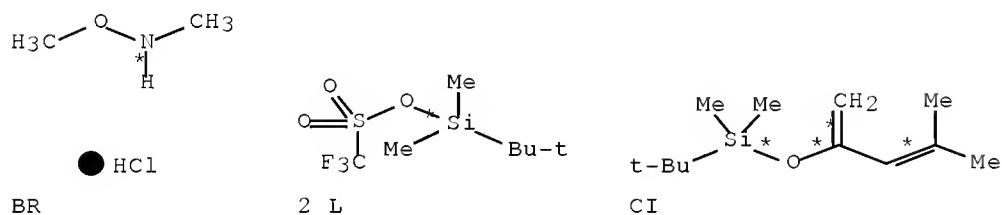
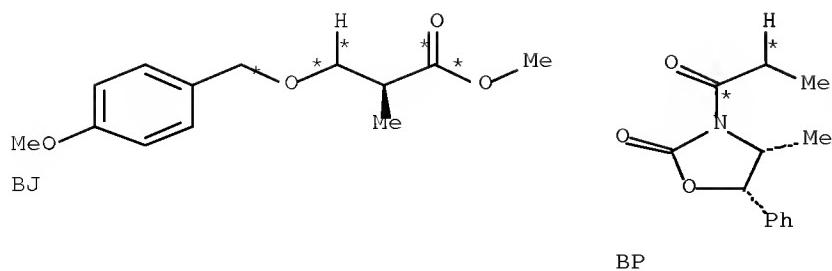
RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

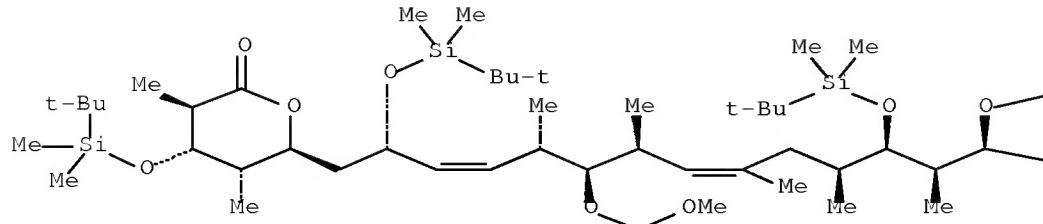
PRO CQ 633293-93-3

RX(324) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)

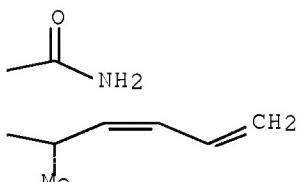
RX(324) BJ + BP + BR + 2 L + CI + CE + AV +
CP ==> CQ



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CO₂
YIELD 92%

- RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF
- RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation
- RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F₃CSO₃BBu₂
PRO BQ 132969-62-1
- RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%
- RX(24) RCT BS 252342-49-7, L 69739-34-0
- STAGE(1)
RGT N 108-48-5 2,6-Lutidine
- STAGE(2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)₂
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH₂C₁₂

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂C₁₂

STAGE(3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et₂O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE (2)

RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂

CON 0 - room temperature deg C

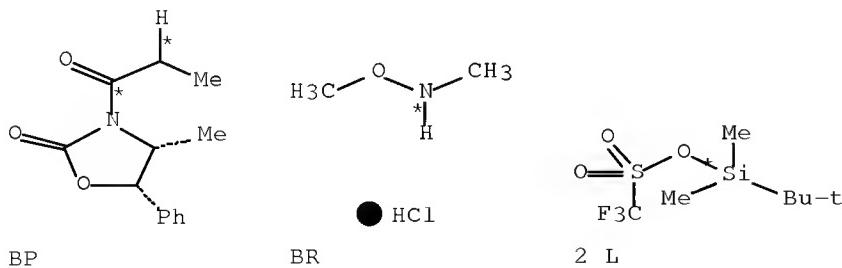
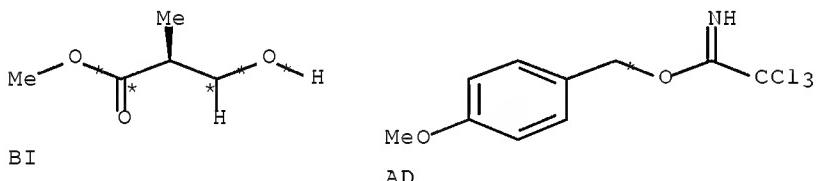
RX(29) RCT CO 633293-76-2, CP 3019-71-4

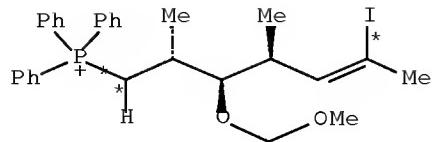
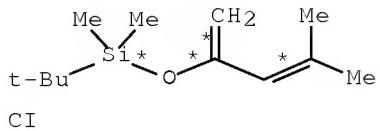
RGT CR 1344-28-1 Al₂O₃

PRO CQ 633293-93-3

RX(326) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28), RX(29)

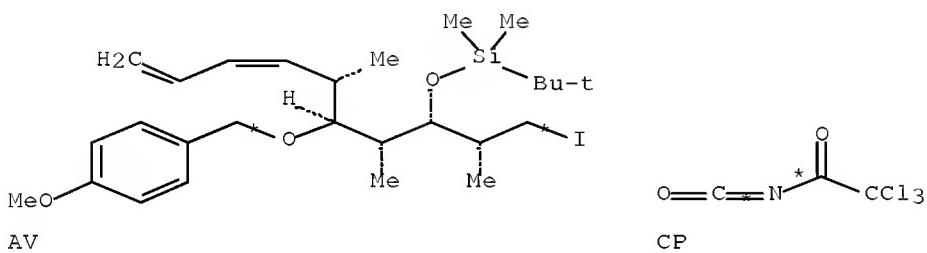
RX(326) BI + AD + BP + BR + 2 L + CI + CE +
 AV + CP ==> CQ





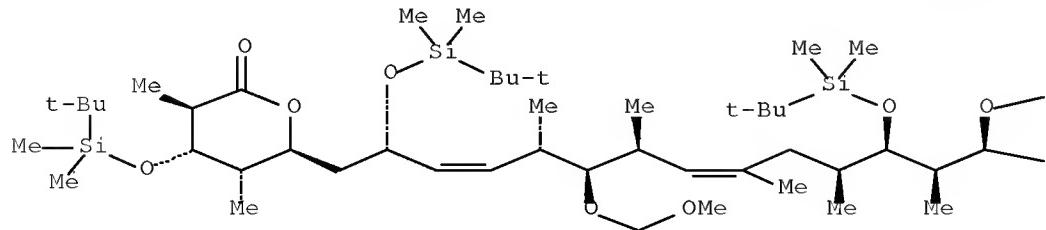
● I⁻

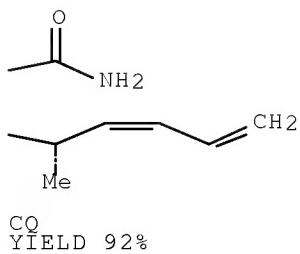
CE



¹³
STEPS
→

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- RX(13) RCT BI 80657-57-4, AD 89238-99-3
 RGT BK 24057-28-1 Pyridinium tosylate
 PRO BJ 132969-71-2
 SOL 75-09-2 CH₂C₁₂, 110-82-7 Cyclohexane
- RX(14) RCT BJ 132969-71-2
 RGT BN 16853-85-3 LiAlH₄
 PRO BM 136320-64-4
 SOL 109-99-9 THF
- RX(15) RCT BM 136320-64-4
 PRO BO 132969-60-9
 NTE Swern oxidation
- RX(16) RCT BO 132969-60-9, BP 77877-20-4
 RGT V 121-44-8 Et₃N, F 60669-69-4 F₃CSO₃BBu₂
 PRO BQ 132969-62-1
- RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%
- RX(24) RCT BS 252342-49-7, L 69739-34-0
- STAGE (1)
 RGT N 108-48-5 2,6-Lutidine
- STAGE (2)
 RGT CG 1333-74-0 H₂
 CAT 12135-22-7 Pd(OH)₂
 SOL 64-17-5 EtOH
- STAGE (3)
 RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)₂
- PRO CF 252342-42-0
- RX(25) RCT CF 252342-42-0
- STAGE (1)
 RGT CK 7550-45-0 TiCl₄
 SOL 75-09-2 CH₂C₁₂

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1

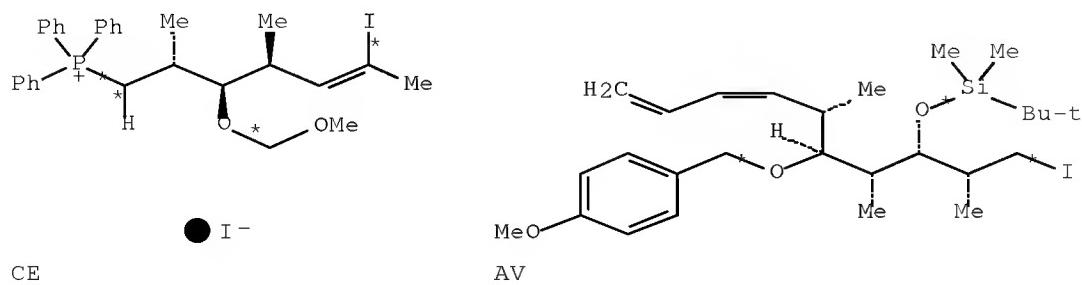
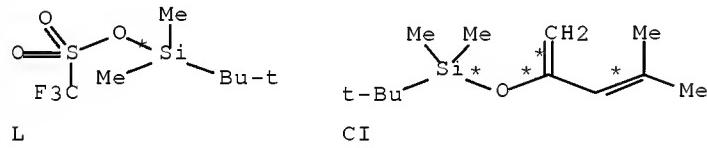
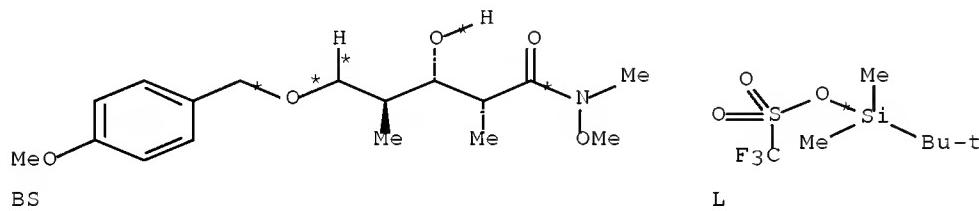
NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

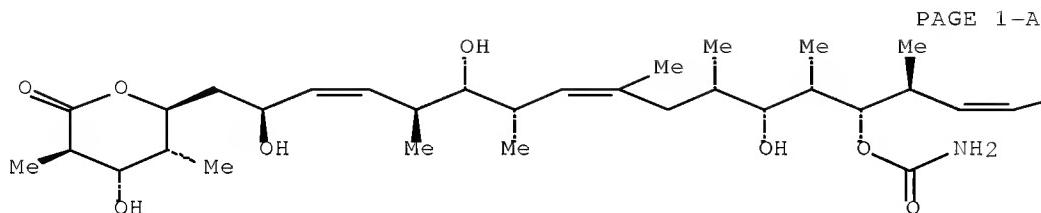
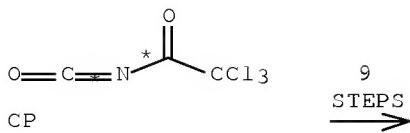
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(348) OF 354 COMPOSED OF RX(24), RX(25), RX(33), RX(26), RX(27), RX(11),
 RX(28), RX(29), RX(30)

RX(348) BS + 2 L + CI + CE + AV + CP ==>
 CS





PAGE 1-B



CS
YIELD 95%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2C12

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

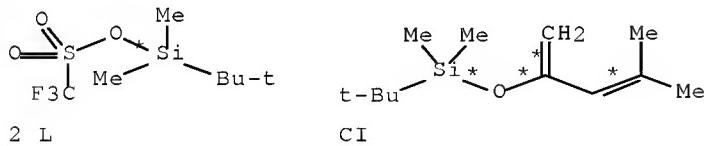
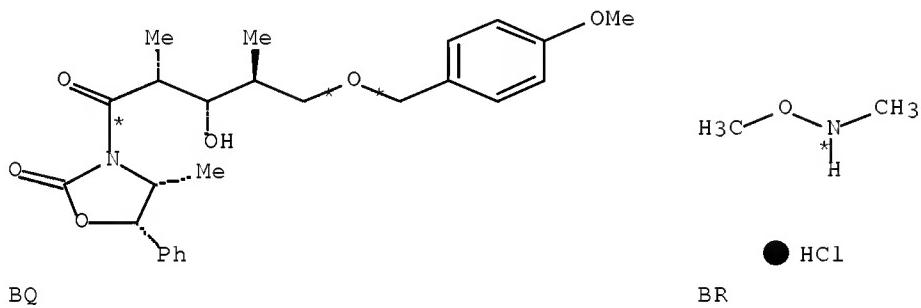
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ

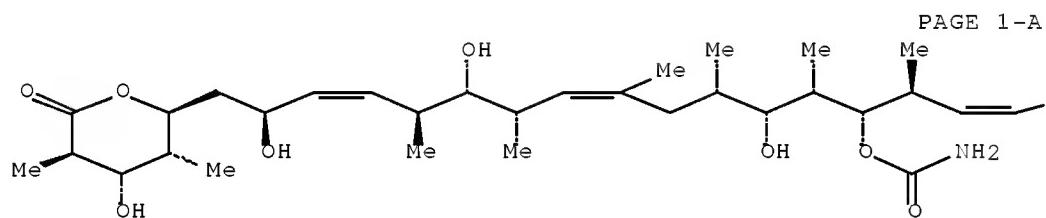
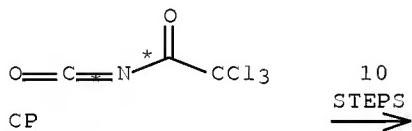
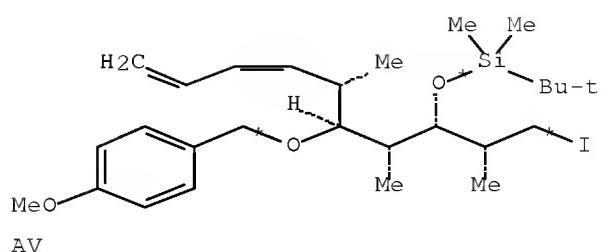
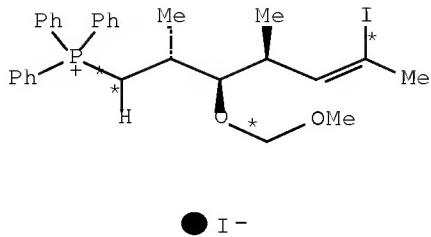
PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(349) OF 354 COMPOSED OF RX(17), RX(24), RX(25), RX(33), RX(26), RX(27),
 RX(11), RX(28), RX(29), RX(30)
 RX(349) BQ + BR + 2 L + CI + CE + AV + CP
 =====> CS





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RX(17) RCT BQ 132969-62-1, BR 6638-79-5
 RGT BT 75-24-1 AlMe₃
 PRO BS 252342-49-7
 SOL 109-99-9 THF
 NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)

RGT N 108-48-5 2,6-Lutidine

STAGE (2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE (3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE (1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE (2)
RCT CI 130043-07-1
CON -78 deg C

STAGE (3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE (1)
SOL 75-09-2 CH₂Cl₂

STAGE (2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE (3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane

CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4

RGT BA 534-17-8 Cs2CO3

CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-

SOL 7732-18-5 Water, 68-12-2 DMF

CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

RX(28) RCT AX 633293-75-1

RGT CC 84-58-2 DDQ

PRO CO 633293-76-2

SOL 7732-18-5 Water, 75-09-2 CH2Cl2

CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4

RGT CR 1344-28-1 Al2O3

PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3

RGT CT 7647-01-0 HCl

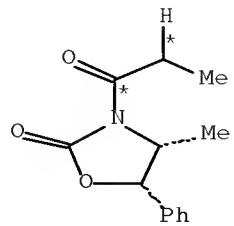
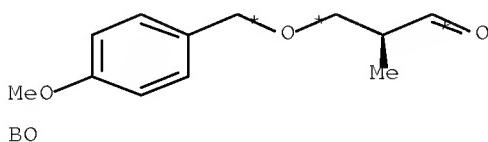
PRO CS 127943-53-7

SOL 7732-18-5 Water, 67-56-1 MeOH

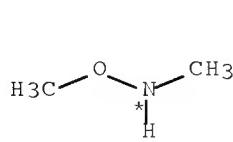
NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(350) OF 354 COMPOSED OF RX(16), RX(17), RX(24), RX(25), RX(33), RX(26),
RX(27), RX(11), RX(28), RX(29), RX(30)

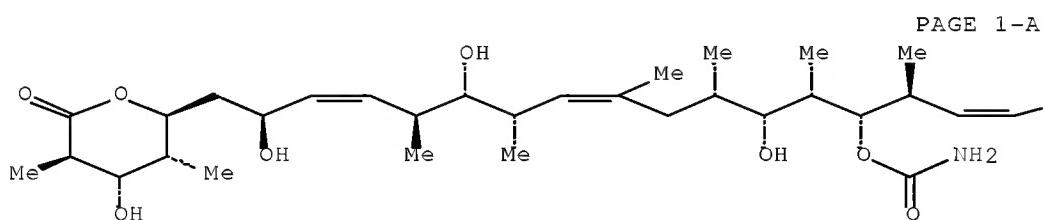
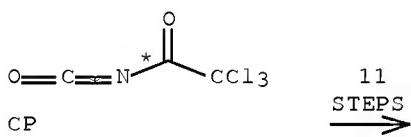
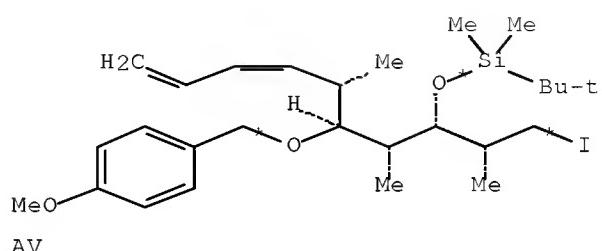
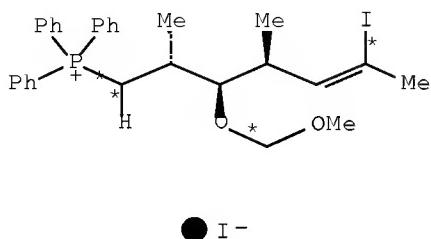
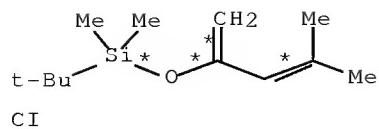
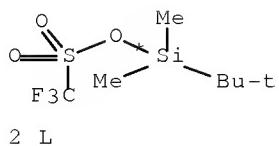
RX(350) BO + BP + BR + 2 L + CI + CE + AV +
CP ==> CS



BR



HCl



PAGE 1-B



CS
YIELD 95%

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2Cl2

STAGE(3)

RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me3Si)2N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)

RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
Pentane
CON SUBSTAGE(1) room temperature -> -78 deg C
SUBSTAGE(2) -78 deg C
SUBSTAGE(3) -78 deg C -> room temperature
SUBSTAGE(4) 1 hour, room temperature

STAGE(2)

RCT AW 850211-74-4
RGT BA 534-17-8 Cs2CO3
CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 7732-18-5 Water, 68-12-2 DMF
CON 20 hours, room temperature

PRO AX 633293-75-1

NTE BBN related byproducts were obtained in 10% yield, Suzuki
coupling

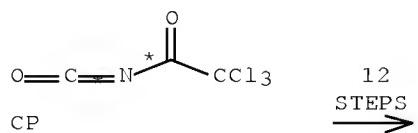
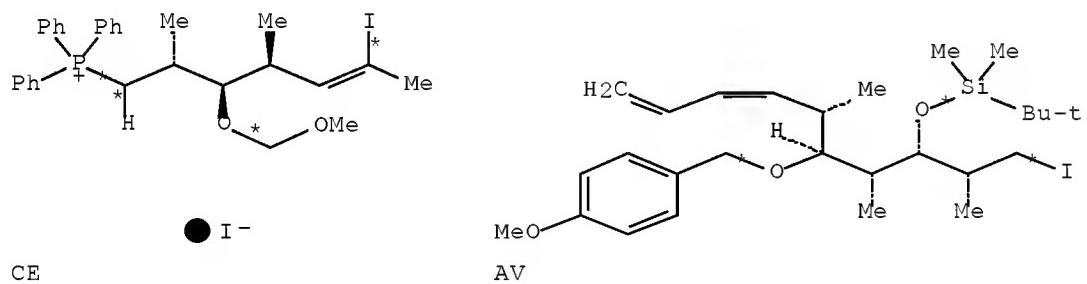
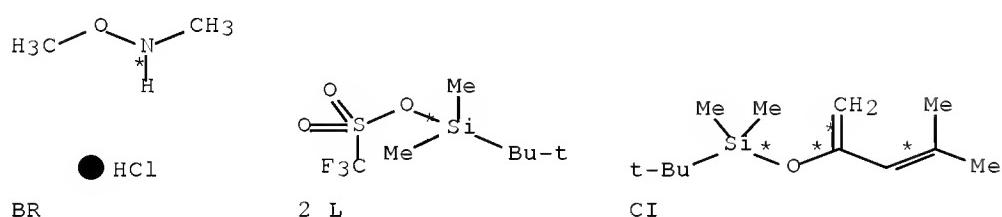
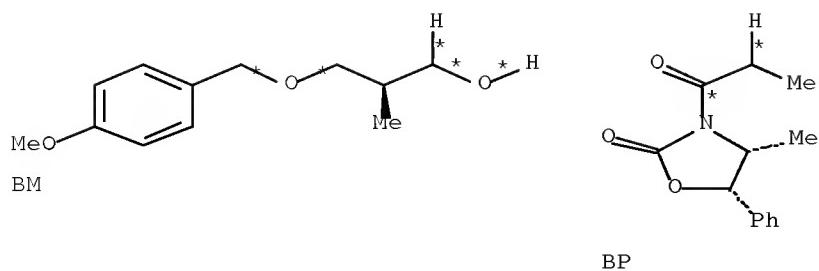
RX(28) RCT AX 633293-75-1
RGT CC 84-58-2 DDQ
PRO CO 633293-76-2
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
RGT CR 1344-28-1 Al2O3
PRO CQ 633293-93-3

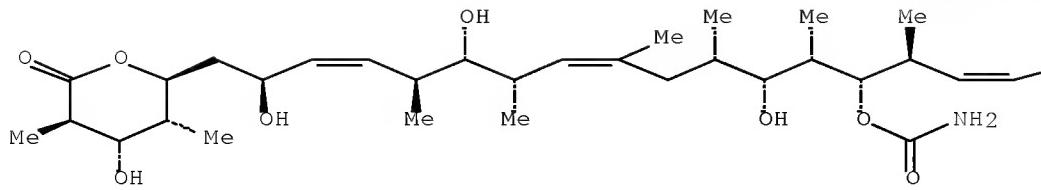
RX(30) RCT CQ 633293-93-3
RGT CT 7647-01-0 HCl
PRO CS 127943-53-7
SOL 7732-18-5 Water, 67-56-1 MeOH
NTE overall yield via iodine substituted pyran-2-one intermediate =
10%

RX(351) OF 354 COMPOSED OF RX(15), RX(16), RX(17), RX(24), RX(25), RX(33),
RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

RX(351) BM + BP + BR + 2 L + CI + CE + AV +
CP ==> CS



PAGE 1-A



PAGE 1-B



CS
YIELD 95%

RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

STAGE(2)
 RCT CI 130043-07-1
 CON -78 deg C

STAGE(3)
 RGT CL 76-05-1 F3CCO2H
 SOL 110-54-3 Hexane
 CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
 RGT CW 54575-49-4 K Selectride
 PRO CM 256920-77-1
 SOL 109-99-9 THF, 108-88-3 PhMe
 NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT AJ 10028-15-6 Ozone
 SOL 75-09-2 CH2Cl2

STAGE(3)
 RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me3Si)2N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

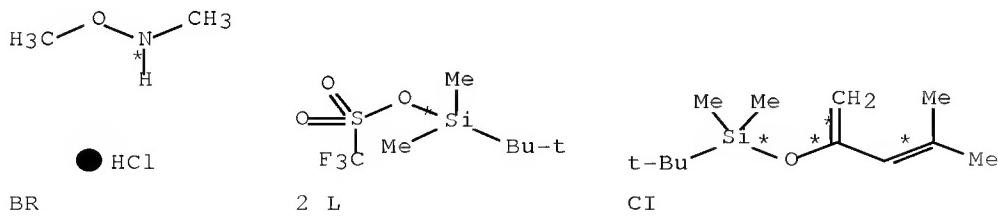
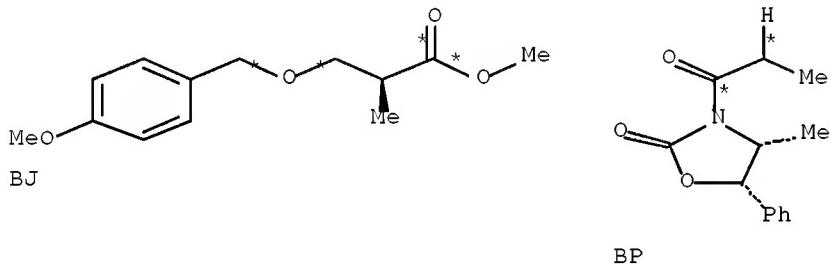
PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki

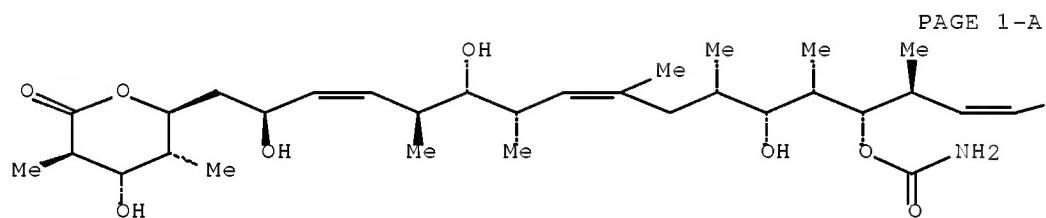
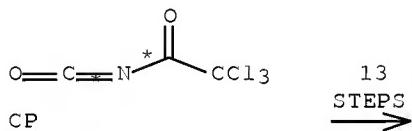
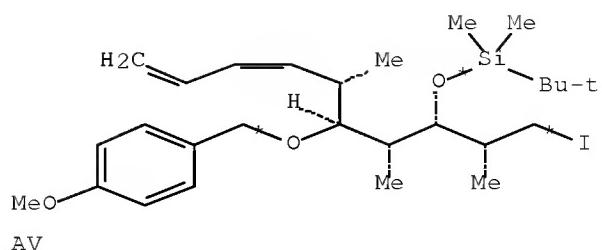
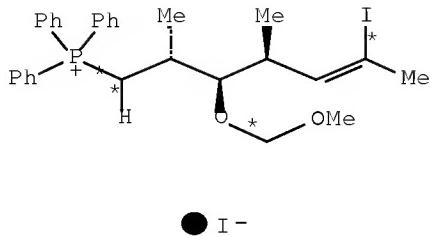
coupling

RX(28)	RCT	AX 633293-75-1
	RGT	CC 84-58-2 DDQ
	PRO	CO 633293-76-2
	SOL	7732-18-5 Water, 75-09-2 CH ₂ Cl ₂
	CON	0 - room temperature deg C
RX(29)	RCT	CO 633293-76-2, CP 3019-71-4
	RGT	CR 1344-28-1 Al2O3
	PRO	CQ 633293-93-3
RX(30)	RCT	CQ 633293-93-3
	RGT	CT 7647-01-0 HCl
	PRO	CS 127943-53-7
	SOL	7732-18-5 Water, 67-56-1 MeOH
	NTE	overall yield via iodine substituted pyran-2-one intermediate = 10%

RX(352) OF 354 COMPOSED OF RX(14), RX(15), RX(16), RX(17), RX(24), RX(25),
RX(33), RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

RX(352) BJ + BP + BR + 2 L + CI + CE + AV +
CP ==> CS





PAGE 1-B



RX(14) RCT BJ 132969-71-2
 RGT BN 16853-85-3 LiAlH4
 PRO BM 136320-64-4
 SOL 109-99-9 THF

RX(15) RCT BM 136320-64-4
 PRO BO 132969-60-9
 NTE Swern oxidation

RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et3N, F 60669-69-4 F3CSO3BBu2
PRO BQ 132969-62-1

RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe3
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%

RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE(1)
RGT N 108-48-5 2,6-Lutidine

STAGE(2)
RGT CG 1333-74-0 H2
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE(3)
RGT U 26412-87-3 Pyridine-SO3 (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE(1)
RGT CK 7550-45-0 TiCl4
SOL 75-09-2 CH2C12

STAGE(2)
RCT CI 130043-07-1
CON -78 deg C

STAGE(3)
RGT CL 76-05-1 F3CCO2H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE(1)
SOL 75-09-2 CH2C12

STAGE(2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH2C12

STAGE(3)
RGT BE 603-35-0 PPh3

PRO CN 252342-51-1
 NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
 RGT CA 1070-89-9 (Me₃Si)₂N.Na
 PRO AW 850211-74-4
 CON -78 deg C -> -10 deg C
 NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE(1)
 RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi
 SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs₂CO₃
 CAT 603-32-7 Ph₃As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki coupling

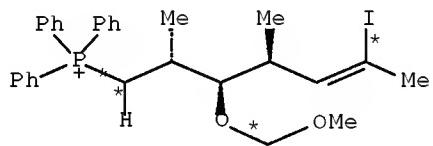
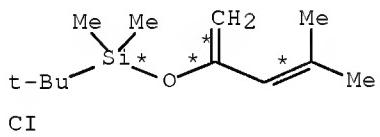
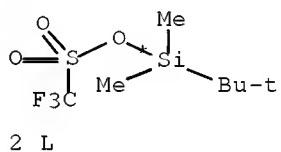
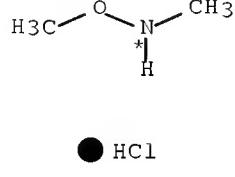
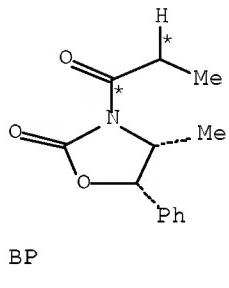
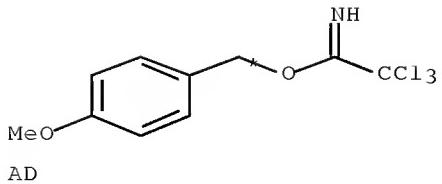
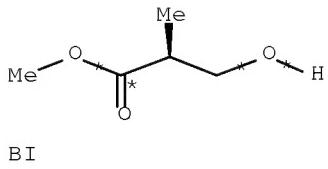
RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH₂Cl₂
 CON 0 - room temperature deg C

RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al₂O₃
 PRO CQ 633293-93-3

RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate = 10%

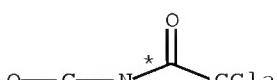
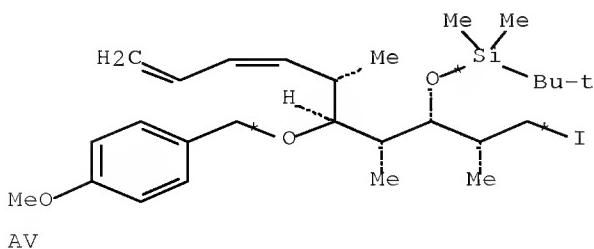
RX(353) OF 354 COMPOSED OF RX(13), RX(14), RX(15), RX(16), RX(17), RX(24),
 RX(25), RX(33), RX(26), RX(27), RX(11), RX(28), RX(29), RX(30)

RX(353) BI + AD + BP + BR + 2 L + CI + CE +
 AV + CP ==> CS

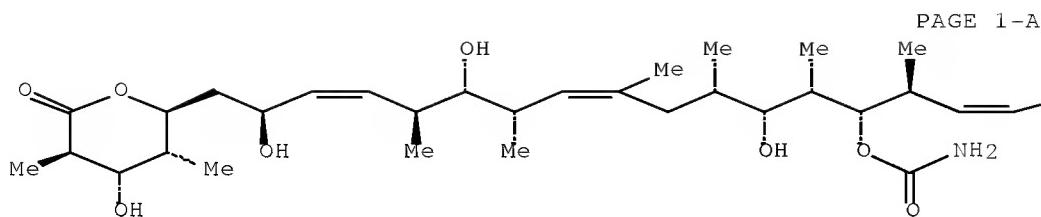


● I⁻

CE



14
STEPS
→



PAGE 1-B



CS
YIELD 95%

- RX(13) RCT BI 80657-57-4, AD 89238-99-3
RGT BK 24057-28-1 Pyridinium tosylate
PRO BJ 132969-71-2
SOL 75-09-2 CH₂Cl₂, 110-82-7 Cyclohexane
- RX(14) RCT BJ 132969-71-2
RGT BN 16853-85-3 LiAlH₄
PRO BM 136320-64-4
SOL 109-99-9 THF
- RX(15) RCT BM 136320-64-4
PRO BO 132969-60-9
NTE Swern oxidation
- RX(16) RCT BO 132969-60-9, BP 77877-20-4
RGT V 121-44-8 Et₃N, F 60669-69-4 F3CSO₃BBu₂
PRO BQ 132969-62-1
- RX(17) RCT BQ 132969-62-1, BR 6638-79-5
RGT BT 75-24-1 AlMe₃
PRO BS 252342-49-7
SOL 109-99-9 THF
NTE yield over 5 steps starting from Roche's ester = 72%
- RX(24) RCT BS 252342-49-7, L 69739-34-0

STAGE (1)

RGT N 108-48-5 2,6-Lutidine

STAGE (2)
RGT CG 1333-74-0 H₂
CAT 12135-22-7 Pd(OH)2
SOL 64-17-5 EtOH

STAGE (3)
RGT U 26412-87-3 Pyridine-SO₃ (1:1), E 7087-68-5 EtN(Pr-i)2

PRO CF 252342-42-0

RX(25) RCT CF 252342-42-0

STAGE (1)
RGT CK 7550-45-0 TiCl₄
SOL 75-09-2 CH₂Cl₂

STAGE (2)
RCT CI 130043-07-1
CON -78 deg C

STAGE (3)
RGT CL 76-05-1 F₃CCO₂H
SOL 110-54-3 Hexane
CON room temperature

PRO CJ 252342-43-1

RX(33) RCT CJ 252342-43-1
RGT CW 54575-49-4 K Selectride
PRO CM 256920-77-1
SOL 109-99-9 THF, 108-88-3 PhMe
NTE stereoselective, ratio of diastereomers = 9:1

RX(26) RCT CM 256920-77-1, L 69739-34-0

STAGE (1)
SOL 75-09-2 CH₂Cl₂

STAGE (2)
RGT AJ 10028-15-6 Ozone
SOL 75-09-2 CH₂Cl₂

STAGE (3)
RGT BE 603-35-0 PPh₃

PRO CN 252342-51-1
NTE yield over 12 steps starting from Roche's ester = 33%

RX(27) RCT CE 850211-72-2, CN 252342-51-1
RGT CA 1070-89-9 (Me₃Si)₂N.Na
PRO AW 850211-74-4
CON -78 deg C -> -10 deg C
NTE stereoselective, Wittig coupling, yield over 13 steps = 20%

RX(11) RCT AV 850211-69-7

STAGE (1)
RGT AY 38050-71-4 9-BBN-OMe, AZ 594-19-4 t-BuLi

SOL 60-29-7 Et2O, 109-99-9 THF, 110-54-3 Hexane, 109-66-0
 Pentane
 CON SUBSTAGE(1) room temperature -> -78 deg C
 SUBSTAGE(2) -78 deg C
 SUBSTAGE(3) -78 deg C -> room temperature
 SUBSTAGE(4) 1 hour, room temperature

 STAGE(2)
 RCT AW 850211-74-4
 RGT BA 534-17-8 Cs2CO3
 CAT 603-32-7 Ph3As, 72287-26-4 Palladium,
 [1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
 (SP-4-2)-
 SOL 7732-18-5 Water, 68-12-2 DMF
 CON 20 hours, room temperature

 PRO AX 633293-75-1
 NTE BBN related byproducts were obtained in 10% yield, Suzuki
 coupling

 RX(28) RCT AX 633293-75-1
 RGT CC 84-58-2 DDQ
 PRO CO 633293-76-2
 SOL 7732-18-5 Water, 75-09-2 CH2Cl2
 CON 0 - room temperature deg C

 RX(29) RCT CO 633293-76-2, CP 3019-71-4
 RGT CR 1344-28-1 Al2O3
 PRO CQ 633293-93-3

 RX(30) RCT CQ 633293-93-3
 RGT CT 7647-01-0 HCl
 PRO CS 127943-53-7
 SOL 7732-18-5 Water, 67-56-1 MeOH
 NTE overall yield via iodine substituted pyran-2-one intermediate =
 10%

L3 ANSWER 9 OF 9 CASREACT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 130:38235 CASREACT Full-text
 TITLE: Total Synthesis of (+)-Discodermolide
 AUTHOR(S): Marshall, James A.; Johns, Brian A.
 CORPORATE SOURCE: Department of Chemistry, University of Virginia,
 Charlottesville, VA, 22901, USA
 SOURCE: Journal of Organic Chemistry (1998), 63(22), 7885-7892
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total synthesis of (+)-discodermolide (I) is described. The approach
 involves assemblage of three key stereotriad subunits through addition of
 nonracemic allenyltin, -indium, and -zinc reagents to (S)-3-silyloxy-2-
 methylpropanal derivs., followed by reduction of the resulting anti,syn- or

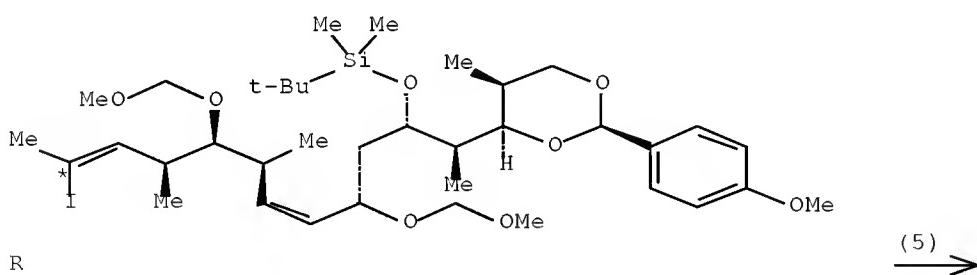
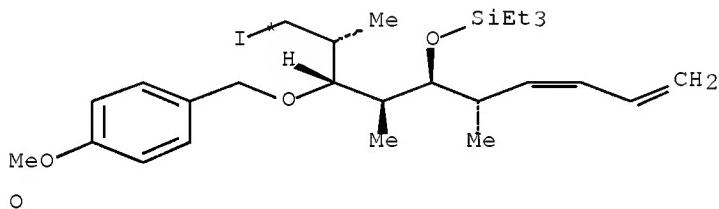
syn,syn-homopropargylic alc. adducts to the (E)-homoallylic alcs. and subsequent Sharpless epoxidn. Addition of Me cuprate reagents or Red-Al to the resultant epoxy alc. yielded the key precursors, (2S,3S,4S)-HC.tplbond.CCH(α Me)CH(β OCH₂OMe)CH(β Me)CH₂OSiEt₃ (II), aldehyde (III), and (2S,3R,4S,5S,6Z)-HOCH₂CH(α Me)CH(α OCH₂C₆H₄-4-OMe)CH(α Me)CH(α OSiEt₃)CH(β Me)CH=CHCH=CH₂ (IV). Addition of alkyne II (as the lithio species) to aldehyde III afforded the propargylic alc. (V) as the major stereoisomer. Lindlar hydrogenation and installation of appropriate protecting groups led to an aldehyde which was converted to the (Z)-vinylic iodide (VI) upon treatment with α -iodoethylidene triphenylphosphorane. Suzuki coupling of this vinylic iodide with a boranate derived from iodide of IV led to the coupled product (VII) with the complete carbon backbone of (+)-discodermolide and the correct stereochem. The synthesis was completed by cleavage of the cyclic PMP acetal at C1 with i-Bu₂AlH and three-step oxidation-esterification to the ester. Cleavage of the C19 Et₃Si ether and C19 carbamate formation followed by cleavage of the remaining alc. protecting groups, first with DDQ and then aqueous HCl, afforded I.

REFERENCE COUNT:

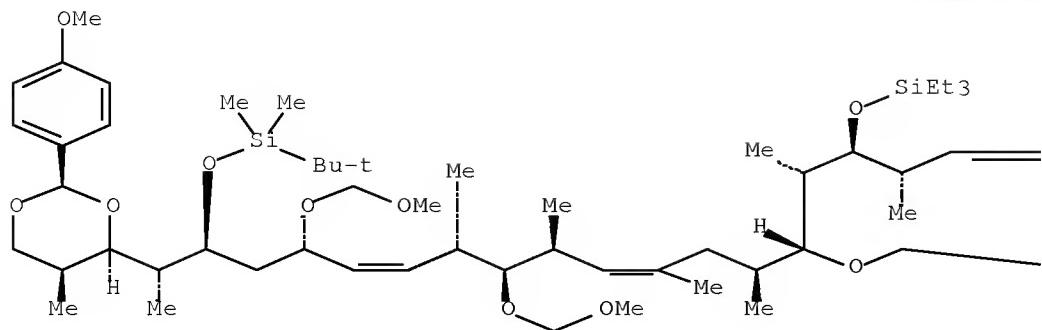
28

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

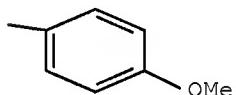
RX(5) OF 7 ...O + R ==> S



PAGE 1-A



PAGE 1-B



S
YIELD 74%

RX(5) RCT O 216669-69-1, R 216669-22-6

STAGE (1)

RGT T 594-19-4 t-BuLi
SOL 60-29-7 Et2O

STAGE (2)

RGT U 280-64-8 9-BBN
SOL 109-99-9 THF

STAGE (3)

RGT V 7789-78-8 CaH2
CAT 72287-26-4 Palladium,
[1,1'-bis(diphenylphosphino- κ P)ferrocene]dichloro-,
(SP-4-2)-
SOL 68-12-2 DMF

PRO S 216669-75-9

=> d his

(FILE 'HOME' ENTERED AT 14:33:15 ON 06 MAY 2009)

FILE 'CASREACT' ENTERED AT 14:33:53 ON 06 MAY 2009

L1 STRUCTURE UPLOADED
L2 0 S SSS L1
L3 9 S SSS L1 FULL

=> s l3 and (ay<2004 or py<2004 or pry<2004)
 80910 AY<2004
 528110 PY<2004
 31094 PRY<2004
L4 2 L3 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d scan

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Synthesis of discodermolide and variants thereof

RX(11) OF 354 - REACTION DIAGRAM NOT AVAILABLE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

ALL ANSWERS HAVE BEEN SCANNED

=> d scan 14 bib ti 1-2
'1-2' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

L4 2 ANSWERS CASREACT COPYRIGHT 2009 ACS on STN

TI Synthesis of discodermolide and variants thereof

RX(11) OF 354 - REACTION DIAGRAM NOT AVAILABLE

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE, Single-step Reactions
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- Indexing data
IPC ----- International Patent Classifications
ISTD ----- STD, indented with text labels
OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 MAX ----- Same as ALL
 PATS ----- PI, SO
 SCAN ----- TI and FCRD (random display, no answer number. SCAN
 must be entered on the same line as DISPLAY, e.g.,
 D SCAN.)
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for
 all single-step reactions)
 STD ----- BIB, IPC, and NCL

 CRD ----- Compact Display of All Hit Reactions
 CRDREF ----- Compact Reaction Display and SO, PY for Reference
 FHIT ----- Reaction Map, Diagram, and Summary for first
 hit reaction
 FHITCBIB --- FHIT, AN plus CBIB
 FCRD ----- First hit in Compact Reaction Display (CRD) format
 FCRDREF ---- First hit in Compact Reaction Display (CRD) format with
 CA reference information (SO, PY). (Default)
 FPATH ----- PATH, plus Reaction Summary for the "long path"
 FSPATH ----- SPATH, plus Reaction Summary for the "short path"
 HIT ----- Reaction Map, Reaction Diagram, and Reaction
 Summary for all hit reactions and fields containing
 hit terms
 OCC ----- All hit fields and the number of occurrences of the
 hit terms in each field. Includes total number of
 HIT, PATH, SPATH reactions. Labels reactions that have
 incomplete verifications.
 PATH ----- Reaction Map and Reaction Diagram for the "long
 path". Displays all hit reactions, except those
 whose steps are totally included within another hit
 reaction which is displayed
 RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
 RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)
 RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
 RXS ----- Hit Reaction Summariers (Map and Summary for all hit reactions)
 SPATH ----- Reaction Map and Reaction Diagram for the "short
 path". Displays all single step reactions which
 contain a hit substance. Also displays those
 multistep reactions that have a hit substance in both
 the first and last steps of the reaction, except for
 those hit reactions whose steps are totally included
 within another hit reaction which is displayed

To display a particular field or fields, enter the display field
 codes. For a list of the display field codes, enter HELP DFIELDS
 at an arrow prompt (=>). Examples of combinations include: D TI;
 D BIB RX; D TI, AU, FCRD. The information is displayed in the same order
 as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,
 FPATH, SPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may
 be used with the DISPLAY command to display the record for a specified
 Accession Number.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d scan 14 bib ti 2
 '2' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

TI Total Synthesis of (+)-Discodermolide

RX(5) OF 7 - REACTION DIAGRAM NOT AVAILABLE

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE, Single-step Reactions
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
IND ----- Indexing data
IPC ----- International Patent Classifications
ISTD ----- STD, indented with text labels
OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

MAX ----- Same as ALL
PATs ----- PI, SO
SCAN ----- TI and FCRD (random display, no answer number. SCAN must be entered on the same line as DISPLAY, e.g., D SCAN.)
SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for all single-step reactions)
STD ----- BIB, IPC, and NCL

CRD ----- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ----- Reaction Map, Diagram, and Summary for first hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ----- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with CA reference information (SO, PY). (Default)
FPATH ----- PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT ----- Reaction Map, Reaction Diagram, and Reaction Summary for all hit reactions and fields containing hit terms
OCC ----- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
PATH ----- Reaction Map and Reaction Diagram for the "long path". Displays all hit reactions, except those whose steps are totally included within another hit reaction which is displayed
RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)

RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
 RXS ----- Hit Reaction Summariers (Map and Summary for all hit reactions)
 SPATH ----- Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

```
=> d scan 14 bib ti
INVALID SCAN FIELD FOR FILE 'CASREACT'
```

One or more of the display fields specified are not valid with DISPLAY SCAN in the current file. Enter HELP DSCAN at the arrow prompt (=>) for the list of fields that may be used when scanning the answers.

```
=> d 14 bib ti 1-2
```

L4	ANSWER 1 OF 2	CASREACT	COPYRIGHT 2009 ACS on STN		
AN	142:411149	CASREACT	<u>Full-text</u>		
TI	Synthesis of discodermolide and variants thereof				
IN	Smith, Amos B., III; Freeze, Brian Scott; Xian, Ming				
PA	The Trustees of the University of Pennsylvania, USA				
SO	PCT Int. Appl., 61 pp.				
CODEN: PIXXD2					
DT	Patent				
LA	English				
FAN.CNT	1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005035489	A2	20050421	WO 2004-US33473	20041012
	WO 2005035489	A3	20050804		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20070276144	A1	20071129	US 2007-575136	20070509
PRAI	US 2003-510097P	20031009			
	WO 2004-US33473	20041012			
OS	MARPAT 142:411149				

TI Synthesis of discodermolide and variants thereof

L4 ANSWER 2 OF 2 CASREACT COPYRIGHT 2009 ACS on STN
AN 130:38235 CASREACT Full-text
TI Total Synthesis of (+)-Discodermolide
AU Marshall, James A.; Johns, Brian A.
CS Department of Chemistry, University of Virginia, Charlottesville, VA,
22901, USA
SO Journal of Organic Chemistry (1998), 63(22), 7885-7892
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
TI Total Synthesis of (+)-Discodermolide
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 14 bib ti 2

L4 ANSWER 2 OF 2 CASREACT COPYRIGHT 2009 ACS on STN
AN 130:38235 CASREACT Full-text
TI Total Synthesis of (+)-Discodermolide
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PB American Chemical Society
DT Journal
LA English
TI Total Synthesis of (+)-Discodermolide
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff h
COST IN U.S. DOLLARS
FULL ESTIMATED COST

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	224.05	224.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
CA SUBSCRIBER PRICE

	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:04:23 ON 06 MAY 2009

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSPTANSC1625

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'CASREACT' AT 15:08:48 ON 06 MAY 2009
FILE 'CASREACT' ENTERED AT 15:08:48 ON 06 MAY 2009
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	224.05	224.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

=> logoff y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	224.05	224.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.02	-7.02

STN INTERNATIONAL LOGOFF AT 15:09:04 ON 06 MAY 2009